PN-AAA-502

93621

AGENCY FOR INTERNATIONAL DEVELOPMENT
OFFICE OF THE SCIENCE ADVISOR
ROOM 320 SA-18
WASHINGTON, D.C. 20523-1818

EVALUATION OF
PROGRAM IN SCIENCE AND TECHNOLOGY COOPERATION (PSTC)
HEALTH BIOTECHNOLOGY

Barbara Sina, Ph.D.
AAAS Diplomacy Fellow
Office of the Science Advisor
November 1988

0173B

B

EXECUTIVE SUMMARY
STUDY OF THE
PROGRAM IN SCIENCE AND TECHNOLOGY COOPERATION (PSTC)
HEALTH BIOTECHNOLOGY PROGRAM

One of the six areas of research funded by the Office of the Science Advisor (AID/SCI) in the Program in Science and Technology Cooperation (PSTC) deals broadly with the application of biotechnology to human and livestock health. Research was begun in 1982 to capitalize on the promise of new approaches to the solution of human health and animal production problems in developing countries. New vaccines, diagnostics tools and therapeutic agents for tropical diseases were emphasized. By 1988, 53 PSTC grants had been given to scientists in this research area. Work had been funded in 22 developing countries.

The project files containing the original research proposal and progress reports were analyzed. Twenty-one completed projects were submitted to external scientific review panels. Many of the developing country laboratories were visited and many grantees presented their work at the PSTC Conference on Biotechnology for Health and Agriculture in Washington D.C. in June 1988. A mail survey questioning the investigators' experience with the program was conducted.

Most of the scientists contacted during the evaluation agreed that PSTC offers a unique opportunity for collaborative research in health biotechnology. Developing country scientists tend to view PSTC as a means for training and technology transfer whereas U.S. scientists tend to view PSTC as adding a vital field study dimension to their laboratory-based studies on tropical disease. The evaluation analysis demonstrated that PSTC health biotechnology projects have produced state-of-the-art research resulting in internationally read publications and subsequent research funding opportunities. PSTC health biotechnology grants have also contributed to strengthening research institutions and potentially produced new tools in the struggle against tropical diseases.

1. Scientific success:

- The majority of the health biotechnology projects achieved a high level of success in meeting their proposed objectives.
- The projects did not, for the most part, stress basic research nor result in conceptual scientific breakthroughs.
- Several projects utilized new biotechnological approaches that resulted in "products" (primarily diagnostic reagents) that are ready for testing of field applicability.

- Most projects reported publications in international scientific journals; there was an average of three journal publications per completed project. Increased developing country authorship could benefit the grantees and better disseminate their research results.

- Several grantees competed successfully for additional projects from PSTC or other international funding agencies.

- The portfolio addresses the tropical disease research priorities designated by the World Health Organization but could better follow the priorities of the 1982 National Academy of Sciences workshop on biotechnology. It might include greater emphasis on tropical veterinary diseases.

- Some PSTC health biotechnology projects are in areas also funded by AID/S&T/Health. In some cases, the PSTC projects complement the S&T/Health projects but a few projects appear to be repetitive efforts.

2. Scientific collaboration:

- The projects involve very highly regarded U.S. and developing country researchers and institutions.

- Total funding is equally divided between the U.S. and developing countries; however, few projects proposed equal financial sharing between collaborators.

- The health biotechnology projects are distributed worldwide. Asia (especially in Thailand) has 46 percent of the projects, Latin America 27 percent , and Africa 9 percent. Many of the projects were in the more advanced developing countries which may be more institutionally capable of basic research.

- The U.S. collaborator played the leading role in the majority of the projects. The U.S. collaborative role involved many relationships from expert consultant, to advanced-degree mentor, to co-experimentalist. All levels of collaboration were found in successful projects, although projects with only a minimal role for one or the other of the collaborators were most problematic.

- From the developing country scientists' perspective, research training was the most effective and sought after element in PSTC projects and most often formed the basis of collaboration. (I thought they liked the money even better than the training!)

3. Scientific capacity strengthening:

- o PSTC funding established apparently sustainable biotechnology laboratories in several developing countries.

- o PSTC projects which successfully demonstrated the potential in biotechnology have encouraged some institutions to expand their biotechnology efforts.

- o Approximately half of the grants studied requested no-cost extensions. The major reason for these requests appears to be delays in initiating the work due to administrative difficulties in obtaining equipment and supplies.

- o Grantees did not perceive increased developing country administrative capacity to be the result of a PSTC grant.

- o AID/SCI review of safety and ethical procedures in the proposed research (i.e., human subjects, recombinant DNA, etc.) appears to have influenced some developing country institutions to set up oversight of these concerns.

4. Administrative support of projects by AID/SCI:

AID/SCI has primarily focused its time and efforts on grant making. Grant management has been assigned to A.I.D. Project Officers in Washington or in missions. Although the majority of the health biotechnology projects were successful with minimal A.I.D. intervention, reviewers suggested more technical/ scientific monitoring might have improved some projects.

A new challenge for AID/SCI is to link research and the application of research "products" such diagnostics, vaccines and therapeutics for developing countries. AID/SCI is exploring their incorporation into A.I.D.-sponsored primary health care efforts, and their further development and application by S&T/Health or biotechnology companies.

E

EVALUATION OF PSTC HEALTH BIOTECHNOLOGY

TABLE OF CONTENTS

F

TABLE OF CONTENTS (continued)

G

LIST OF TABLES

LIST OF APPENDICES

I. INTRODUCTION

The Office of the Science Advisor (AID/SCI) was established in 1980 to administer the Program in Science and Technology Cooperation (PSTC) with a mandate to:

1. Support worldwide research efforts on critical development problems.

2. Strengthen the capacity of developing countries to perform scientific and technological research and experimentation required for national development.

3. Increase the exchange of expert scientists and engineers between countries.

Basically, PSTC, through supporting and promoting research in developing countries, aims to assist in transforming them from consumers to producers of technological solutions to their own problems in health, food production, etc.

AID/SCI primarily fulfills its mandate through the PSTC competitive grants program which invites scientists from developing countries, in collaboration with U.S. scientists, to submit proposals in several areas of research. The proposals are judged by expert external peer review on the criteria of scientific merit, innovation, relevance to development and their potential to enhance developing country research capabilities. Approved projects are funded for up to $150,000 over two or three years.

From its inception, AID/SCI recognized the promise of biotechnology to provide new vaccines, diagnostic tools and chemotherapeutic agents for the tropical diseases that plague developing countries. Research efforts remain especially critical when old technological solutions to tropical diseases are failing. The problems of increasing pathogen drug resistance, increasing vector pesticide resistance, the lack of low cost, heat stable vaccines and centralized health care delivery systems overwhelmed by expense and expanding, needy populations can begin to be addressed by appropriate biotechnology research.

PSTC offers a unique opportunity for U.S. and developing country scientists to collaborate in applying biotechnology to tropical disease problems. This collaboration is critical to the success of this type of research because:

1. At this time the U.S. is considered the world leader for developing new biotechnology.

2. The U.S. biotechnology industry which recently began to market biomedical applications of this new technology is

driven by profit motive and is not likely to focus on products affordable for use on the diseases of developing countries.

3. Although there are revived U.S. academic laboratory efforts to study tropical disease, a recent National Academy of Sciences study[1/] showed that the U.S. capacity to deal with tropical diseases is "barely adequate." The study found that the U.S. is especially weak in clinical and field tropical disease research (epidemiology and vector ecology). While developing countries are often lacking in the infrastructure, advanced training, etc., required for state-of-the-art basic biomedical research, they are usually strong in clinical and field capacities.

4. Tropical diseases are often difficult to study in the U.S. due to the lack of good animal models for the diseases and the lack of access to patients suffering from these diseases.

Therefore, it appears that only a high level of collaboration between U.S. and developing country scientists can insure that biotechnology applications for tropical diseases are generated. In addition, such collaboration offers training opportunities to both U.S. and developing country participants.

The Biotechnology/Immunology module was specifically designed to promote the technical goal of using new immunological biotechnology approaches to produce vaccines, diagnostic tools and immunotherapy agents for tropical animal and human diseases. In 1982 a workshop convened by the National Academy of Sciences recommended several human and animal diseases for high priority for funding in this module[2/]. Since 1983, the following definition of the Biotechnology/Immunology module has been included in the preproposal guidelines: "Biotechnology/ Immunology in human and/or animal systems, includes recombinant microbiology (genetic engineering), monoclonal antibodies and related immunological techniques for better and more rapid diagnosis, immunotherapy, vaccine development and related health

---

1/ The U.S. Capacity to Address Tropical Infectious Disease Problems, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1987

2/ Priorities in Biotechnology Research for International Development, proceedings of a workshop, July 26-30, 1982, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1982

applications." At the end of the 1988 fiscal year 53 grants had been given under the Biotechnology/Immunology module (list appended).

PSTC not only supports the specialized personnel involved in research but provides some of the infrastructure required for biotechnology research. Biotechnology research requires relatively little sophisticated equipment, but it uniquely requires a supply of relatively expensive, labile biochemical reagents (such as restriction enzymes and monoclonal antibodies). An individual PSTC grant can provide adequate support to initiate a sustainable biotechnology laboratory in a developing country institution as detailled in trip reports of visits to PSTC funded laboratories in Africa, Asia and South America.

It is difficult to establish a direct connection between innovative research and measurable developmental impacts for the two to three year PSTC health biotechnology projects. PSTC seeks to support all the components necessary for catalyzing good research leading to developmental impact. This evaluation will focus on four issues affecting optimal scientific research in PSTC and how AID/SCI has responded to these issues:

1. PSTC was designed to do high quality scientific research which is both innovative and appropriate to solving developing country health problems. Therefore, the scientific success of the health biotechnology projects was evaluated.

2. PSTC emphasizes collaboration between U.S. and developing country scientists as a mechanism to achieve its goals. Therefore, scientific collaboration was evaluated for the projects.

3. An ulterior motive of PSTC is to strengthen science and technological capacity in developing countries. Therefore, the impact on the developing country components (equipment, supplies, administration, safety protocols, bibliographic resources) required for research were evaluated.

4. AID/SCI not only serves as a financial channel for research grants but is empowered to serve in several supportive roles to positively influence the success of the projects funded. Therefore, AID/SCI's role in promoting scientific progress in the projects was evaluated.

II. MATERIALS USED FOR EVALUATION

The following five different strategies were employed to evaluate the PSTC health biotechnology grants funded through 1986 (reports mentioned for each of these activities are appended):

A. FILE REVIEWS

AID/SCI maintains a file containing all the pertinent scientific and administrative documentation for each funded grant. During the last six months of 1987, the files of the more than 300 funded PSTC grants and the computer data base used for tracking them were brought up to date. Materials were organized and missing documents were identified. Letters were sent to project officers and investigators to obtain overdue or misplaced progress reports. As a result of this process, new procedures have been implemented in the office to improve the maintenance of the large volume of information kept on file for funded projects with the aid of computer records.

The following file documents for the health biotechnology grants were particularly useful for the evaluation:

Project Proposal

The project proposal submitted by the principal investigator(s) defined the specific objectives of the project and provided a scientifically detailed workplan. The collaborative contributions of the U.S. and developing country scientists are described and their curriculum vitae are attached. The proposal also contains an itemized budget for each of the contributing laboratories which is justified in terms of the needs of the project.

Grant Agreement

The grant agreement is an administrative document which contains an abstract of the proposal, a budget outline and the A.I.D. requirements for the investigator including a reporting schedule. The funding start date is specified, but the completion date is often amended due to an investigator's request for a no-cost extension.

Correspondence

All the files contain the peer reviewers' provisos and comments to the proposal and the investigators' responses. In addition, the correspondence for any given grant often deals with a variety of administrative matters impacting on progress in the scientific work. Occasionally, a trip report from an A.I.D. source or a project officer's comments may be included.

Progress and Final Reports

According to the grant agreement, the principal investigators are required to submit a progress report and a financial status report every six months and a comprehensive final report at the completion of the project.

These file documents were used for background knowledge of the projects, extraction of some specific data and distributed to the peer reviewers for analysis.

B. SITE VISITS

Several of the laboratories receiving PSTC funding were visited by Dr. Barbara Sina and Dr. Janet Rice (or other A.I.D. staff in conjunction with their travels). Site visits were planned in the countries receiving the highest number of projects encompassed by the evaluation. The visits were informal and usually consisted of a one-to-two-hour discussion with the developing country investigator (sometimes joined by lab members involved in the project) and a tour of the facilities. Discussions focused on the status of the work, scientific and administrative problems encountered and the relationship with A.I.D. Trip reports described the findings of individual site visits (appended). The information gathered does not lend itself easily to quantitation but provided valuable insight into the real impact of the PSTC grants and the workings of the projects.

C. MAIL SURVEY

In order to gather more information from the participants involved in the PSTC biotechnology projects, a survey was distributed to the developing country principal investigator and his/her U.S. counterpart. The survey queried the investigator's experience and opinions on training, safety, research capacity strengthening, collaborative, beneficial and problematic aspects of the program as well as asking recommendations for AID/SCI. The responses were compiled and analyzed in a detailed report (appended) by a statistician with Patricia Fischer Harris at Devres, Inc., who also coordinated the Conference for PSTC biotechnology grantees described below.

D. PSTC GRANTEE CONFERENCE

A four day conference was organized in June, 1988 where U.S. and developing country grantees working on biotechnology projects in health and agriculture were invited to present their results. Washington area academics, A.I.D. project officers and other interested A.I.D. staff were also invited to attend. Abstracts of the presentations were collected (appended). Dr. Irvin Asher prepared a report (appended) on the conference based on the observations by A.I.D. staff, NAS/BOSTID staff and former peer reviewers attending the conference and a survey of the participants (appended). The objectives of the conference went beyond the aims of the evaluation to provide informal peer review, information exchange and general networking among those attending. In addition, presentations and roundtable discussions were held on issues and needs that surfaced in the other components of the evaluation (transcripts appended). The conference served the evaluation primarily to help evaluators

update progress in the projects and to meet with investigators not contacted by other means.

E. PEER REVIEW OF COMPLETED PROJECTS

In July, groups of Washington area scientists were convened and asked to review completed health biotechnology projects in their areas of expertise. Completed projects selected for review were those that contained sufficient progress reports for complete analysis and those that were sufficiently related in subject matter to permit convening appropriately sized discussion panels of reviewers. Two to three reviewers were assigned to intensively analyze each file's progress reports and relevant correspondence in relation to the original proposal and judge how successful the investigators were in meeting their proposed objectives. Each panel of reviewers also commented on the grant's impact, AID/SCI's performance and generally discussed the future role of biotechnology in PSTC. The reviewers' written and spoken opinions were compiled in a report which was passed on to the investigators of each project (appended). The results of six additional projects were reviewed as part of peer review evaluation of follow-on proposals.

III. CHARACTERIZATION OF THE GRANTS EVALUATED

A. GRANTS INCLUDED IN THE EVALUATION

The Biotechnology/Immunology module is defined in the AID/SCI preproposal guidelines as research in "human and animal systems including genetic engineering, monoclonal antibodies and related immunological techniques for better and more rapid diagnosis, immunotherapy, vaccine development and new techniques for rapid epidemiological assessment and related health applications." By strict interpretation of what types of research constitute immunological biotechnology, nine of the designated grants in the module contain no immunological work (also see table 9). The majority of these nine grants are using molecular biology techniques either to study the basic biology of the pathogen or to develop new diagnostic tools. In reviewing whether proposals fit into this module, A.I.D. does not add to the the strict interpretation of their definition of biotechnology/immunology and generally considers all experimental health research appropriate. AID/SCI designation (in their data base) of what constitutes Biotechnology/Immunology appears to have varied somewhat from year to year. Two other modules have projects tangentially related to biomedical research. The Chemistry for World Food Needs module contains a few human and animal nutrition projects. The Biological Control module encompasses a large number of tropical disease vector control projects but the Biotechnology/Immunology module also includes six grants focussing on vector biology. Forty-eight PSTC projects are included in this evaluation (Table 1), forty from the designated Biotechnology/Immmunology module and eight health-related grants

gleaned from other categories. Two projects from the Biological Control module were included in the evaluation because they involve genetic engineering to produce a bioinsecticide specifically for malaria-carrying mosquito species. The evaluation also includes chemotherapy projects found in the Biotechnology/Immunology and Genetics (mostly biological diversity projects) modules or designated as "Other." Only five Biotechnology/Immunology grants involve veterinary disease. Due to the blurred character of the Biotechnology/Immunology module and the suitability of reviewing non-modular but biomedical projects in a related context this evaluation of PSTC health biotechnology projects will embrace a somewhat broader scope of research than the original module definition implies.

B. GRANTS COVERED BY VARIOUS EVALUATION METHODS

Table 1 contains a list of all the grants included in the study. The table specifies the ways in which each grant was individually evaluated in addition to a review of the grant's file. Twenty-nine percent (29%) of the projects were studied by three methods and 10% by the maximal four methods suggesting that these results reflect a balance of scientific critique and participant viewpoint of the program. Thirty-one percent (31%) of the projects were studied by two methods but 88% of these projects were site visited and/or peer reviewed, considered to be the most thorough methods. Twenty-seven percent (27%) of the listed grants were only evaluated by one method (91% by site visit or peer review) which may bias the interpretation of the results of the project particularly where no direct contact was made with the investigators. It must be remembered that a variety of factors influenced the methods used to study these projects. For example, only the thirty grants had reached completion and therefore were eligible for peer review. Twenty one grants in total were peer-reviewed. Location was a large determinant of whether a project could be conveniently visited. Countries with the largest number of biotechnology grants, such as Thailand, Peru, and Kenya, were selected as well as neighboring countries with only a few grants. Fifty-eight percent (58%) of the projects were visited by Dr. Barbara Sina, Dr. Janet Rice or others. While the survey response represents 42% of the listed projects, in no case were surveys recovered from both U.S. and developing country investigators.

C. COMPARISON OF BIOTECHNOLOGY/IMMUNOLOGY TO OTHER MODULES

AID/SCI has consistently funded more Biotechnology/Immunology grants over the years in comparison to the other research modules. As shown in Table 2 most of the modules represent about 12% of the total grants but Biotechnology/Immunology at 18% averages over twice the number of the lowest populated modules. Although the percentage of Biotechnology/Immunology prepproposals received each year averages 10% (overall ranking fourth among the modules), 20% of these are eventually funded (ranking third).

This may suggest that the quality of the Biotechnology/Immunology proposals is higher than those submitted in other modules. In contrast, the Chemistry module which ranks second to Biotechnology/Immunology in the percent of total PSTC grants funded each year, ranks first among the modules for the percent of preproposals received but fifth when the percentage of preproposals funded is considered. For this module, the percentage of total preproposals received parallels the percentage that eventually are funded. But the two-fold difference in this ratio for Biotechnology/Immunology grants is surpassed by the five-fold difference seen for the Plant Biotechnology and biological control modules (which rank third and fourth, respectively, in the percent of total PSTC grants and represent the lowest number of submitted proposals). Therefore, it can be argued that these results reflect some measure of the quality of the proposals, AID/SCI emphasis on the various modules within the program and possibly other factors.

The preproposal guidelines inform submitters that AID/SCI allocates approximately $1 million to each of the research modules annually. AID/SCI makes no specific efforts to balance each year's categories of preproposals it receives, but does try, in a limited fashion, to balance the number of grants among the modules each year. The priority ranking of grants by the scientific peer reviewers is used as a guide by AID/SCI in adjusting the balance of grants to be funded among the modules. For example, AID/SCI may only fund the approved proposals given highest priority in an overrepresented category but may fund lower priorities in underrepresented modules.

During the 1988 grant cycle the post-peer review funding decisions made by AID/SCI produced the following results. Although Biotechnology/Immunology proposals submitted in 1988 received the highest level of approval by the peer review, as shown in Table 3, subsequent AID/SCI decisions on priority projects for funding this year resulted in the lowest percentage of grant obligations compared to other modules. Plant Biotechnology proposals suffered similarily during this process.

The office maintains a policy of rejecting proposals approved by peer reviewers and never approving projects rejected by peer reviewers. If the quality of the review is questioned external scientific review is obtained. Overall, thirteen decisions (nine approvals and 4 non-approvals) made by the peer reviewers in October 1987 were reconsidered by AID/SCI. Most of the modifications merely detailed the possibility of funding until the subsequent year. Biotechnology/Immunology proposals were affected by four of these modifications.

Peer review has approved more proposals in recent years than AID/SCI has been able to fund. Increasing numbers of proposals are held over each year for possible funding in the next year's cycle. The 1988 cycle was unusual in that more than half of the

proposals funded were actually recommended for approval by peer review in previous years. The addition of these grants skewed the total distribution among modules considerably. Biotechnology/Immunology, similar to the other modules, represented 12% of the approved proposals submitted in 1988 but only 7% of the total grants obligated this year.

The 1988 funding cycle may be atypical. It appears that Biotechnology/Immunology proposals are conferred superior approval by the scientific peer reviewers but AID/SCI may subsequently indirectly discriminate against these proposals to achieve a more balanced distribution among modules. Because higher priority ranking proposals are funded, the Biotechnology/Immunology module may have more potential for success.

D. REGIONAL DISTRIBUTION

The regional distribution of health biotechnology grants generally reflects the grant distribution seen in the total PSTC program. The Asia and Near East region represents almost half of the participants in this category (Table 4). Thailand has been remarkably successful in the PSTC proposal competition. Thailand has received one-fourth of the health biotechnology grants, predominating since 1985. No PSTC health projects were established in Nepal, Pakistan or Sri Lanka which have significant A.I.D. programs and other PSTC grants.

The Latin America/Carribean region received approximately one-third of the health grants. Peru, the second largest PSTC participant after Thailand, has steadily won five health grants since 1983. Recent funding in Peru has been disrupted by Brooke Amendment sanctions. 36% of the Latin American region's PSTC health projects are located in the "advanced developing countries" of Mexico, Brazil and Venezuela "graduated" by A.I.D. A.I.D no longer maintains a substantial presence in these countries. Only one health project was approved in the Caribbean Island countries and one in Central America.

The African region has maintained a low but steady acquisition of health biotechnology grants. Predictably, the more advanced countries of Kenya and Cameroon represent approximately half of this effort. The capacity to conduct many more health research projects exists throughout Africa as shown by the participant lists for the XII International Congress for Tropical Medicine and Malaria (summarized in Table 5) and the OCCGE International Conference on New Measures in Malaria Control (African Trip Report).

E. PRINCIPAL INVESTIGATORS

The principal investigator for a grant is usually the scientist who submitted the PSTC proposal. For record keeping purposes

AID/SCI usually designates as principal investigator the collaborator at the institution receiving the grant which subsequently issues a subcontract to the other collaborator. But in some cases A.I.D. has directly obligated funds to both collaborators. The status of principal investigator does not necessarily indicate receipt of the majority of the grant budget but it does carry the responsibility for reporting on the progress in the project.

Approximately 60% of the principal investigators for the health biotechnology grant were from developing countries (table 1). Twelve developing country principal investigators had no U.S. collaborators. Half of these grants were in Thailand. The principal investigator in the Papua New Guinea project was an Australian expatriate and a Filipino principal investigator collaborated with an Australian. The other grants lacking U.S. collaborators were in Peru, Mexico and Jordan. Two-thirds of these proposals were submitted in 1985 and 1986.

PSTC is not actively or aggressively advertised in the United States. Because of the goals of PSTC, AID/SCI has tried to avoid a flood of U.S.-based proposals, and instead has concentrated on promoting submission of good proposals from developing country scientists. The U.S. scientists most familiar with PSTC grants are most likely those who participate without compensation in the peer review process each year, primarily from the Washington area. NIH, Johns Hopkins University and other area institutions have large tropical disease research programs, and participate in the review of health biotechnology grants each year. It may be significant that almost half of the U.S. principal investigators in health biotechnology are from Washington area institutions (table 1). Harvard University, for example, has a tropical disease research program equivalent to Johns Hopkins but contributes only one principal investigator in health biotechnology. Four grants were made in 1982 and 1983 to U.S. investigators without developing country collaborators (table 1) based on a policy that they were working on significant developing country health problems. Since this time the inclusion of a developing country collaborator has been required by AID/SCI.

F. RESEARCH AREAS

The health biotechnology research within PSTC is limited to addressing diseases that primarily affect human and animal health in the tropics. As seen in Table 6, PSTC has provided funding for research in a wide variety of tropical diseases. 70% of the PSTC health biotechnology grants fund research in the six human diseases that the World Health Organization has deemed as priorities (malaria, schistosomiasis, filarial disease (including onchocerciasis), trypanosomiasis (African sleeping sickness and

Chagas' disease), leishmaniasis and leprosy)[4/]. Other U.S. donors, such as the Rockefeller Foundation, also provide research funds for these diseases [4/].

A.I.D./S&T/Health funds basic tropical disease research in the Diatech and Malaria Vaccine programs. The Malaria Vaccine research program is narrowly mandated to its announced goal. Diatech funds projects to develop immunological, molecular biological and other techniques for the diagnosis of malaria, diarrheal diseases acute respiratory diseases and tuberculosis (Table 7). Both S&T/Health programs provide funding almost exclusively to U.S. scientists in much greater amounts than PSTC. To insure non-overlapping but complementary funding AID/SCI requires health sector council review of preproposals before the investigators are requested to submit full proposals.

By project title, it appears that some common research objectives may exist between PSTC and the S&T/Health research programs. This is especially apparent for PSTC malaria, tuberculosis and diarrheal disease projects. Three of the seven PSTC malaria projects involve chemotherapy which should, by definition, be excluded from the S&T/Health research programs. But one Malaria Vaccine program contract is provided to clone the pyrimethamine resistance gene from Plasmodium falciparum. And one Diatech project involves developing an ELISA for the measurement of plasma quinine levels. The remaining four PSTC malaria projects do involve vaccine and/or diagnostic related research but appear to have similar scientific goals to the S&T/Health projects which may result in complementarity or repetition.

Diatech funds several projects to develop monoclonal diagnostic reagents for enteropathic E. coli, Giardia, Entamoeba and Salmonella. PSTC is also funding five grants which involve monoclonal antibody production to three of these pathogens. Both Diatech and PSTC have funded the development of a monoclonal field assay for tuberculosis. Although Diatech does not give priority to Onchocerciasis and Leishmaniasis, they are funding diagnostics development in these diseases, as is PSTC. It is unclear whether the development of multiple monoclonal antibodies for a given organism represents complementary approaches to the best product or duplication of effort.

AID/S&T/Agriculture funds some basic biotechnology research in animal disease. Only the babesiosis vaccine PSTC grant appears to coincide their efforts until reagents are compared. The Biotechnology/Immunology module was specifically designed to promote a technical goal, i.e., the use of new immunological

---

4/ Tropical Disease Research, a Global Partnership at Work: New Approaches to Research Capacity Strengthening, UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases, First Edition, 1988

biotechnology approaches to producing vaccines, diagnostic tools and immunotherapy agents for tropical diseases. In 1982 a workshop was convened by the National Academy of Sciences to advise A.I.D. on priorities in biotechnology[2/]. Eight human and four animal diseases as well as one zoonotic disease where recommended as high priority for vaccine research funding based on:

1. Current availability of an effective, inexpensive, safe vaccine

2. Feasibility of using biotechnology approaches to develop better, cheaper, and safer vaccine candidates within five years

3. Current funding available in sufficient amounts from sources other than A.I.D. considered in relation to the relative importance of the disease in developing countries

4. Public health significance (human disease) or economic losses (animal diseases)

As shown in Table 8, 44% of the PSTC biotechnology projects being evaluated fulfill the NAS recommendations[2/]. Additional grants to work on diseases not represented in Table 8 have been added to the PSTC portfolio during the subsequent 1987 and 1988 funding cycles. Overall, approximately half of the health biotechnology projects involve immunological approaches to diagnostics and/or vaccines in their objectives (table 9). Immunological and DNA based diagnostics represent the goals of approximately half of the projects. Chemotherapy, basic biology and miscellaneous biotechnology projects comprise about a third of the grants evaluated.

IV. EVALUATION ISSUES

A. SCIENTIFIC SUCCESS

1. PEER REVIEW OF COMPLETED PROJECTS

Peer review of twenty-one completed health biotechnology grants provided the most thorough analysis of the success investigators had in meeting their scientific objectives. Three panels of 7-9

2/ Priorities in Biotechnology Research for International Development, proceedings of a workshop, July 26-30, 1982, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1982

U.S. scientists each were convened to examine completed projects, respectively, in viral and bacterial disease, parasitic protozoan disease, and helminthic disease. Although evaluating success is subjective, the reviewers were usually quite consistent in their views of a given project. 57% of the health biotechnology projects were judged to be mostly or fully successful in achieving the objectives originally proposed (Table 10). 33% were judged to be partially successful and only 10% were thought to have failed. The reviewers thought that 75% of the work was of good to excellent quality. No projects were judged to be without scientific merit. 62% of the projects were regarded as making a good to excellent contribution to the state-of-the-art in their field. Overall, the reviewers were laudatory toward the majority of the health biotechnology projects they evaluated.

The peer review panels were also asked to assess each project's impact in terms of international development. 48% of the projects were found to be good to excellent in capacity strenthening for the developing country participants. Six projects were judged to be poor in this aspect primarily due to the lack of inclusion of developing country scientists. Although there was a great deal of discussion about whether, generally, health biotechnology will contribute to international development, the reviewers thought that on an individual basis 62% of the projects produced potential benefits in the struggle against tropical disease. In comparison, the reviewers' opinions were somewhat equivocal when their ratings of various projects for scientific success were matched to cumulative success ratings which includes the aspects of capacity strengthening and benefit to international development (table 11). Five projects which ranked in the top eight for scientific success maintained top ranking when their overall achievement was evaluated. Three projects with high scientific ranking dropped out of the top eight when overall success was considered, primarily because no developing country collaborator was involved. Three projects with high cumulative rankings were not included in the top eight scientifically successful projects. The investigator for one of these projects, rated among the lowest eight in scientific success, was denied a subsequent PSTC grant in two competitions. On the low end of the ranking scale, six out of the eight lowest ranking projects scientifically were also rated among the lowest overall.

2. COMPLETED PROJECTS NOT PEER REVIEWED

Nine projects were completed in time for the July peer review but were not included for various reasons. Three project files did not contain enough progress reports to permit a full scientific analysis. Two projects' topics of research did not lend themselves to any of the three panels for discussion. The investigators from the four remaining projects submitted follow-on proposals to PSTC competition. AID/SCI provided reviewers of those subsequent submissions with the previous project's progress

reports. Therefore, in effect, these four projects have already been evaluated scientifically. If the reviewers' decisions reflect the influence of the investigator's previous work, two of the projects could be considered successful (new proposals were approved) and two were unsuccessful (new proposals were disapproved).

3. PUBLICATIONS

Publication is regarded as a measure of scientific success because it indicates that enough data was collected to answer a scientific question or scientifically describe a phenomenon and the published data is subjected to critical review by other experts who approve its authenticity. PSTC grantees are asked to submit to AID/SCI all publications stemming from their grants and to acknowledge A.I.D. support in them. U.S. investigators, especially, tend to cite multiple sources of support in a paper and, therefore, it is difficult to determine A.I.D.'s exact contribution. Table 12 summarizes the reported publications accounted for in the AID/SCI files (list appended). Overall 54% of the grants reported publications. But approximately one-third of the health biotechnology projects are ongoing and often publication occurs at the completion of the project. The incidence of publication increases to 67% when only completed projects are considered. This works out to an average of 2.7 publications per grant or 4.4 publications per completed grant.

Scientific journal articles represent 67% of the total reported publications, scientific meeting abstracts/papers 28% and review articles/book chapters 5%. Papers in international journals are generally regarded as the most respected type of scientific publication in biomedical research due to their required scientific detail, thorough scientific review and accessibility to the scientific community which lends itself to independent confirmation of the results. 86% of the reported journal articles were in international journals. Overall, each completed grant reported an average of three scientific journal publications. 39% of the projects produced 1-2 journal articles, 39% of the projects produced 3-6 articles and 11% produced 7-9 articles.

These publication statistics drop significantly when only publications including developing country authors are calculated. The total percent of grants with developing country authored publications drops to 31%. Twice as many exclusively U.S. authored journal articles and meeting publications were reported and seven times as many book chapters/review articles. Developing country scientists represent only 35% of the total authors listed on the reported publications. Table 12 compares the number of developing country authored scientific journal articles by region. On average, one developing country authored journal article was produced per grant. The number of Asian authored papers (48% of developing country authored papers) is

equivalent to the Asian proportion of PSTC health biotechnology grants (46%). Latin American authorship is higher than expected when compared to Latin America's share of grants. On the other hand, African authorship is less than half what would be expected. AID/SCI currently offers no support other than financial for promoting publication from the PSTC projects.

4. FOLLOW-ON FUNDING

Another indicator for scientific success is the ability to obtain subsequent funding. The investigator survey found that 83% of the respondents intended to continue their work in biotechnology based on the results they obtained during their PSTC project. Those who said they would not continue the work cited lack of funding as the principal obstacle. 92% of the respondents said they would consider writing another PSTC proposal. Strictly speaking AID/SCI does not fund follow-on research. Investigators must submit a new proposal to the annual review process which encompasses new steps in their research, a discrete activity that is not repetitive of their previous project. Investigators from eight health biotechnology grants have been approved for subsequent PSTC grants (some have not yet received funding).

In order to gain more information concerning the dynamics of PSTC, health biotechnology investigator participation during the history of the program was examined in detail. All preproposals submitted to the program were surveyed for submissions by health biotechnology investigators (table 13). Forty-three percent (43%) of the U.S investigators and 40% of developing country investigators applied multiple times to PSTC. The success rate was 56% for multiple applicants from either the U.S. or developing countries. (Approximately one-fourth of the multiple applicants were successful in receiving funding on their second attempt. The remainder represent follow-on applications.) This is significantly higher than the 10% preproposals, on average, which eventually receive funding each year.

Table 13 compares the success of the U.S. and developing country investigators submitting second PSTC grants at various decision points during the grant review process. In the sequence of review decision points leading to funding, only 25% of all incoming preproposals are approved by AID/SCI and A.I.D. sector council for submission of full proposals. But approximately 50% of the follow-on health biotechnology applications are approved to this point. Thirty-one percent (31%) follow-on proposals from U.S. investigators are funded compared to 22% from developing country investigators. Significantly, 33% follow-on proposals from developing country investigators are approved by peer review but are not yet funded compared to only 6% from U.S. investigators. However, this may be an indication of the greater barriers to obligating grant funds in developing countries compared to in the U.S.

In the early years of PSTC, AID/SCI was discouraging of follow-on grants. AID/SCI now accepts follow-on applications for "selected LDC investigators who may recompete for funding in subsequent, regular PSTC review cycles" (preproposal guidelines) but follow-on grant policy has not yet solidified.

Several successful developing country PSTC grantees have gone on to receive funding from other sources. Three investigators reported receiving NIH grants, two won Rockefeller fellowships, two found WHO support for their programs and one investigator has a McConnell-Clark grant. A few have gained funding from other international donor agencies. As explained in the Asian trip report, many Thai investigators with PSTC grants receive limited matching funds from the Thai government. These examples illustrate how PSTC success is correlated with additional opportunity for scientific funding.

5. RESEARCH PRODUCTS READY FOR FIELD TESTING

Participants in the site visits, peer review and survey are asked to identify successful "products" of research that were ready to move towards application. Peer review and site visits identified ten projects with "products" potentially ready for experimental field testing (table 14). The majority of these products are diagnostic tools. Two are potential chemotherapeutic agents. The metal leaching strains, produced from a project somewhat anomalously grouped with the Biotechnology/Immunology module, are currently being tested on mining wastes with support from Peruvian industry (South American Trip Report).

When biotechnology grantees were asked by the survey how their results could best be utilized to help improve health or agriculture in developing countries, 80% recommended field testing and 35% indicated development for large scale application. The grantees most frequent survey response to the question of how AID/SCI could promote the best utilization of their results was to provide funding for continuing research. AID/SCI has not defined a consistent strategy for assuring that basic research products move towards application. Follow-on field testing proposals to test the applicability of new research "products" often border on the type of research, i.e., PSTC specifically excludes "surveys or evaluations, baseline data collection or routine mapping" (preproposal guidelines). To date there are no PSTC health biotechnology projects which have been directly "picked up" by S&T/Health for continued support for application and integration into ongoing health development programs as originally envisioned.

B. SCIENTIFIC COLLABORATION

Collaboration between U.S. and developing country scientists is considered the cornerstone for PSTC. In its preproposal guidelines, AID/SCI now requests strong collaborations with true

"intellectual partnership" and warns that preproposals fail because they do not appear to have the full involvement of a developing country investigator. "Ideally projects will involve a principal investigator from a developing country with a U.S. collaborator. They will visit each other's laboratories and coordinate closely in order to transfer advanced research techniques to target countries." The guidelines are careful to point out that "technology transfer cannot be the goal of a proposal outside the framework of a scientific project but training and travel may be included to achieve the purposes of collaboration during the research project." Despite emphasis in PSTC, U.S. collaboration is optional for developing country participants.

1. BASIS OF COLLABORATION

A wide variation in the collaborative relationships exists in the PSTC health biotechnology projects (table 15). The projects were reviewed to determine the format of collaboration proposed. The most widely proposed mechanism of collaboration involved training a developing country scientist in the U.S. counterpart laboratory (28%). Training was selected as the mechanism of collaboration in half of the projects where only one type of exchange was proposed. The other half, predominantly Thai projects, included only minimal involvement by a U.S. consultant. Overall, U.S. consultancy was the second most requested form of collaboration (19%). Obtaining access to biomedical research materials rare in either the U.S. or developing country constituted the other most likely basis of proposed collaboration (developing country samples 10%, U.S. samples 14% or developing country field work 12%) but never the only basis of collaboration. 68% of the health biotechnology proposals included one or two forms of collaboration and the remainder mostly three forms. Only rarely was parallel experimentation in both labs proposed which implies a major/minor partnership. In 61% of the grants the U.S. participant appeared to play the lead role in the project in terms of control over the progress of the work. This contrasts to the fact that 60% of the projects have developing country principal investigators.

In order to assess the success of collaboration, the type of collaboration proposed for each project was compared to that achieved as conveyed in progress reports and site visit discussions. Sixty-one percent (61%) of the projects appeared to fulfill their proposed collaborative responsibilities, 14% appeared only partially successful and 25% of the collaborations appeared to have failed. In five out of the seven cases of failure, the collaboration was only minimally defined in the proposal. Division of labor and work plan schedule were missing or vague. It should be noted that in some cases the proposed terms of collaboration changed to achieve the same ends. For example, when a Burmese participant was not permitted to leave the country, the U.S. collaborator provided similar training in

Burma instead of in his lab. In a few cases, unexpected contributions occurred. For example, a U.S. consultant additionally provided standards and chemical analysis for a Peruvian collaborator. Interestingly, whenever the U.S. collaborator proposed to work in the developing country for training, field collection or actually living there for an extended time, the commitment was achieved. Other types of collaboration had approximately a 50-60% success rate. Two projects involving four or five forms of collaboration were completely successful compared to those with less proposed partnership. Not surprisingly, the success of any collaboration depends primarily on the commitment of the participants. But it appears that AID/SCI has maintained an inconsistent standard of collaboration when reviewing proposals. While aiming primarily to benefit the developing country participants via U.S. collaboration, some proposals were approved which were primarily beneficial to the U.S. labs with developing country scientists playing a minor or negligible role. In addition, AID/SCI has not developed mechanisms to monitor, support or assure their funded collaborations.

2. COLLABORATION AND BUDGET

In addition to a required statement elaborating the roles of the collaborators, the proposal budget reflects aspects of the collaboration (table 16). Only 25 of the health biotechnology proposals specified funds for both collaborators even though 36 proposals name collaborators. In eleven grants only 1-10% of the total budget is set aside for one of the collaborators. Less than 20% of the grants result in 30-70% financial sharing. But overall, U.S. and developing country participants averaged approximately equal proportions of the health biotechnology budgets (44% and 56%, respectively). 14 projects provide 0-10% of the budget to the developing country collaborator. Half of these projects represent grants given from 1981-1983 when the AID/SCI collaboration requirement was optional for U.S. investigators. 20 projects provide 90-100% of the budget to the developing country collaborator. 15 of these projects were obligated in 1985-1986 and half are located in Thailand. There appears to be a growing trend toward developing country control over PSTC grant budgets.

The results of the scientific peer review of completed projects were matched to the portion of their budget devoted to the developing country collaborator. This was done in an attempt to see how the level of funding shared between collaborators influenced the success of the project. Table 16 demonstrates that there is no apparent correlation between the level of developing country funding in a given project and its success scientifically or including international development aspects.

3. COLLABORATION AND TRAVEL

AID/SCI views travel expenses requested in the project budget as indicative of the collaboration proposed. For all health biotechnology grants, travel averaged 9% of the proposed budgets (table 17). Fifty-two percent (52%) of the grants evaluated proposed joint U.S.-developing country budgets. The U.S. share of jointly budgeted grants averaged 28% for travel compared to 15% for developing countries. There were no travel funds requested in five U.S. and five developing country portions of joint budgets. Four joint budgets contain funds only for U.S. travel and two have funds only for developing country participant travel. Interestingly, travel represented more than 50% of the total funds in the U.S. share of 10 joint budgets compared to 3 developing country shares. In terms of funding, travel seems to be a more predominant aspect for the U.S. collaborators.

Three episodes of travel per health biotechnology project were reported by both U.S. and developing country respondents to the survey. This fits AID/SCI's unwritten minimum recommendation of one travel exchange for each year of a grant. But surprisingly, the survey showed that half of the travel contacts made by either party occurred before the grant was funded.

Data collection and consultation were ranked among the most frequent reasons given by both collaborators for travel (survey appended). U.S. participants travelled as much for writing as for data collection and consultation whereas writing was the least frequent reason given for developing country participant travel. Developing country participants, primarily M.Sc. and graduate students, travelled most frequently for training. Clearly travel represents a critical interaction within a collaborative project, although the motives for travel by U.S. and developing country participants frequently differ. It is difficult to extract the impact of travel contact on an individual project by any means other than personal interviews (see trip reports). AID/SCI does not formally require trip reports from investigators and this interaction is rarely described in progress reports.

4. COLLABORATION AND SALARIES

The salaries itemized in a project's budget probably reflect the minimum number of participants in the research. Many other participants received salary from their institution or other sources, especially principal investigators. Overall, U.S. and developing country investigators devote similar portions of their share of a joint budget for salary (40% and 38%, repectively). But one-fourth of the U.S. budgets do not request salary. And due to extremely different labor costs many more developing country participants are paid from their share of the PSTC budget. Typically, the U.S. counterpart will request salary for one technician or postdoctoral fellow whereas the developing

country partner will request salary for several students and technicians and possibly a portion of the principal investigator's salary to lessen teaching/clinical responsibilities. The exact number of active participants was difficult to gauge from any of the other materials AID/SCI collects for each project. Progress reports almost never indicate who contributes to the work. Depending on custom, only participants of certain rank may be cited as authors on publications. Lack of up-to-date knowledge of participants sometimes leads to confusion in investigator interactions with AID/SCI.

A more reliable account of participation may be obtained from the survey which asked for a list of personnel from the respondent's institution that were involved in the project. From the small sample of respondents, it appears that approximately three times as many developing country scientists on average were involved in each health biotechnology project as U.S. scientists (table 18). Two-thirds of the U.S. participants had advanced degrees whereas a little less than half of the developing country participants did. No U.S. graduate student participants were reported. In contrast, graduate students represent one-fourth of the developing country participants. The U.S. effort averaged one technician per project whereas the developing country effort averaged two technicians.

The survey also specifically asked which personnel were trained in the new techniques of antibody production, protein purification, recombinant DNA and tissue culture as part of the research efforts. Overall, approximately equal numbers of participants at all degree levels were trained in new techniques and all the aforementioned techniques were equally popular. On average half of the participants were reported to have received training. These results confirm that PSTC projects provide significant opportunities for technology transfer via collaborative research. Indeed, survey respondents, asked to explain how the PSTC project affected the participants, thought they primarily gained from their training experience. And the desire for more training support was expressed by the greatest number of respondents when asked how PSTC could be more effective.

5. THE COLLABORATION EXPERIENCE

The survey permitted respondents to give voice to their experience with PSTC research collaboration. The survey asked how the collaboration was initiated. 58% said the principal investigator initiated the project, 30% said the co-investigator initiated it and 11% noted that a government or regional institution stimulated the project. Most of the collaborators had previously worked together or at least knew each other personally before submitting to PSTC. 60% felt that both they and their collaborator had contributed appropriate amounts to the project but 47% of the developing country respondents described

their participation as too great. Overall, most respondents rated themselves and their collaborators effective to very effective in the project.

The most common complaint about U.S. collaborators mentioned during the visits to developing country laboratories was a lack of communication. In one section of the survey grantees were asked to indicate the substantial contacts made with their collaborator by phone, letter or in person during various stages of the proposal process. Overall, U.S. collaborators reported 2.5 times as many contacts per person as their developing country counterparts. Correspondence was used twice as frequently for communication by either collaborator as were phone calls or visits. 60-70% of the contacts reported by either collaborator occurred before funds were obligated. Although not reported as the most significant problem encountered, seven developing country scientists (three in Africa and four in Thailand) indicated in the survey that isolation from the scientific network posed difficulties in their research project that in one case (African) stopped the work entirely. These observations may explain the sense of isolation, overburdening or lack of communication some developing country participants described during the course of their PSTC project.

C. SCIENTIFIC CAPACITY STRENTHENING

PSTC grants enhance many other components, in addition to training, that are likely to result in increased scientific capacity. A PSTC grant can set up a fully functional biotechnology facility (trip reports). Indirectly, PSTC grants can also influence the administrative capability and scientific direction in a developing country institution. One interesting example of this involves AID/SCI concern with the potential hazards of laboratory research, many of which are regulated and routinely monitored in the U.S. but only rarely formally dealt with in developing countries. For example, the institutions receiving PSTC funding in Thailand have initiated ethical review committees in response to AID/SCI requests involving human subjects, recombinant DNA, etc. (Asian Trip Report). PSTC grants represent a unique opportunity for developing country scientists to freely direct resources to needs they perceive in order to strengthen their own research capacity.

1. EQUIPMENT AND SUPPLIES

On average, 38% of the total health biotechnology grant funds were appropriated for equipment and supplies in developing country laboratories. In contrast, U.S. collaborative budgets propose drastically less (17%). In fact, 64% of the U.S. collaborative portions do not request funding for equipment and 33% do not request funding for supplies. This probably reflects a greater need in developing countries which are often initiating biotechnology research and collaborating with more established U.S. biotechnology laboratories.

A majority of the health biotechnology survey respondents thought that PSTC had greatly enhanced their laboratory equipment and facilities. But problems with equipment and supplies were the most frequently cited incidents that delayed or stopped research in developing countries. Problems with the process of ordering, shipping and customs accounted for a large number of delays and unexpected expense (trip reports). Currency exchange is often difficult when purchasing U.S. equipment with grant given to the developing country scientists. Some investigators mentioned that because of very high inflation rates in their countries in recent years, delays in AID/SCI obligation of funds sometimes meant that inadequate amounts had been budgetted for required equipment and supplies (trip reports). This financial bind forced new decisions on how resources could be used to meet the objectives of the project and in some cases posed restrictions that could not be overcome. Some developing country investigators mentioned that it was much less expensive to purchase materials in the U.S. and ship them to their country than to buy the same U.S. products from home. Typically, difficulties in obtaining equipment and supplies delayed the initiation of research for six months to a year in developing countries and were the major reason for grant extension requests. In an extreme case, an investigator in Sierra Leone received equipment in July 1988 for a grant which was funded in August 1985 and which was due to terminate in November 1988.

Although not specifically quantitated in this evaluation, the maintenance and repair of equipment in developing countries has long been recognized as a formidable problem.[5/] Some grantees specified budget funds for this purpose. Occasionally, PSTC funds permitted the repair of long unused equipment (trip reports). Some investigators show great ingenuity in coping with equipment problems. When faced with a unrepairable centrifuge for over a year, one Peruvian investigator devised a method of subcellular material isolation that did not require a centrifuge. Some investigators mentioned that donor agency restrictions sometimes make equipment maintenance and repair more difficult. For example, African scientists can more easily obtain equipment from Europe and have trained technicians and metric based spare parts for British, French or Germany brands but not for U.S. brands. Therefore, U.S. purchase requirements imposed by A.I.D. required acquisition of equipment that was difficult for these labs to maintain. In another example, equipment maintenance was impaired because each piece of equipment previously purchased in a lab visited in Bolivia was from a different country with a manual in a different language from Japanese to Hungarian. Although PSTC grants require the purchase of U.S. equipment, waivers can be obtained. Grantees

---

5/ Purchase, Use and Maintenance of Scientific Equipment in Developing Countries, J.F. Gallard and S. Quatter, Interciencia, Vol 13, No. 2, March-April 1988

are apparently not aware of this option. AID/SCI recognizes this is a problem for their grantees and is working indirectly with other organizations to overcome it. AID/SCI previously funded the NIH Biomedical Engineering and Instrumentation division to develop technical and institutional capacity to repair and maintain sceintific equipment in the Carribean. AID/SCI is currently working with the American Association for the Advancement of Science (AAAS) and the Instrumentation Society of America to devise a new support program for this critical component.

2. BIBLIOGRAPHIC RESOURCES AND PUBLISHING SUPPORT

On average, 1-2% of grant funds were requested for bibliographic and publishing support but 50% of both U.S. and developing country investigators made no such request. The lack of a technical library was a frequent complaint of developing country scientists which brought research delays (survey). Libraries in developing country institutions visited were often closed or contained little or dated scientific materials (trip reports). It appeared that few developing country scientists used PSTC funds for scientific journal subscriptions. But it was generally observed that during the conference BOSTID publications and technical and informational materials supplied by AID/SCI rapidly evaporated. AID/SCI has recognized that the lack of bibliographic resources has affected the quality of the research possible in developing countries and is working with other organizations to ameliorate this problem. AID/SCI continues to work with NAS/BOSTID to generate useful publications and with AAAS in their scientific journal distribution program in Africa.

It is difficult to pinpoint the barriers to publication that exist for developing country scientists. The peer reviewers recommended publication of the results from the majority of the developing country participants. But site visit discussions revealed a general reluctance to publish for a variety of reasons. The poorer institutions lacked copiers, photographic facilities and computers which are considered quite essential by U.S. scientists today for partaking from and contributing to the scientific literature. AID/SCI does not require budgetting for publication/bibliographic capabilities and has left the issues and process of publication in the hands of the grantees.

3. INSTITUTIONAL CAPACITY

AID/SCI postulates that the experience of handling a PSTC grant enhances the administrative capabilities to handle other extramural scientific funding. But the majority of the developing country health biotechnology respondents felt no change occurred in the administrative capacity in their lab (50%), department (60%) or institution (71%). AID/SCI receives little feedback concerning the administrative impact of its

grants. In countries receiving large numbers of PSTC grants such as Thailand or Peru, the A.I.D. mission becomes responsible for determining administrative links with the various funded institutions. As mentioned in the Asian and South American trip reports, these missions recently conducted audits of grants to local institutions. The audits resulted in recommendations for their administrative systems and internal control procedures to help comply with A.I.D.'s terms and conditions. One of the barriers repeatedly encountered in developing country institutions is the lack of experience setting up and maintaining separate accounts for PSTC grants. Many developing countries have instituted foreign currency exchange policies that complicate the use of collaborative PSTC funds. A variety of country-specific mechanisms have been tried to simplify the purchase of equipment and supplies and travel between collaborators. AID/SCI is developing a handbook for PSTC grant project officers where collection of management strategies will be described. Some research institution administrators mentioned that A.I.D. seems to have quite different administrative requirements than other international granting agencies.

Institutional overhead costs average 12% of the PSTC health biotechnology proposal budget. Overhead rates in developing countries (10%) average almost three times less than at U.S. institutions (27%). Surprisingly, 53% of the U.S. budgets and 41% of the developing country budgets did not request overhead expenses. No data is available as to what impact the provision of institutional overhead had on administrative capacity strengthening.

The site visits revealed a variety of institutional strengthening efforts related to PSTC grants:

- Inter-institutional collaborations: In Peru and Thailand several local research institutions, previously rivals, have collaborated on PSTC projects.

- Collaboration with Health Programs: In Lima, grantees in the Microbiology/Parasitology Department of Universidad Peruana Cayetano Heredia are working with PRISMA, a primary health care project in the pueblo jovens to study diarrheal disease. Grantees at Chiang Mai and Mahidol Universities collaborate with the Thai Ministry of Health to provide and test malaria diagnostic reagents.

- Institutional collaboration mechanisms: The director at KEMRI in Nairobi prefers to set up a memorandum of understanding with collaborating institutions to insure a constructive relationship. In Kenya, strong institutional mechanisms may be more critical because the A.I.D. Mission is able to provide only minimal administrative support to PSTC grants.

- Research Administrators: The director of Centre Universitaire des Sciences de la Sante at the University of Yaounde, a former PSTC grantee, was recently appointed Vice Chancellor. He has encouraged the younger CUSS scientists to obtain PSTC grants. A computer data base of all scientific equipment at the University has been developed under his auspices which is used to coordinate research and avoid duplication in grant proposal budgets. A similar system is operated in the Rector's Office at Chiang Mai University in Thailand. The Director of the Tropical Medicine Institute at Universidad Peruana Cayetano Heredia has also played an instrumental role in coordinating PSTC proposals and supporting the progress of research projects there.

- Institutional Training Collaboration: The University of Nairobi has a number of graduate programs but limited research facilities. PSTC grants have provided a mechanism for students to be trained at the Kenyan national research institutions or in the U.S.

- Institution Building: Because of the increased research level at Universidad Peruana Cayetano Heredia in Lima, new research facilities are being built. Cameroonian investigators are currently moving into a newly organized Biotechnology Research Center at the University of Yaounde. Receipt of a PSTC and an NIH program grant have promoted the building of a new biotechnology research laboratory at the Ministry of Health in Belo Horizonte, Brazil. Many of the African investigators indicated that PSTC supported their efforts to establish their own institutions as opposed to working under the auspices of the remaining colonial institutions in their countries. It appears that PSTC grants can play a critical role in enhancing a developing country institution with supportive investigators, administrators and facilities.

4. REGIONAL BIOTECHNOLOGY CENTERS

In order to determine directions AID/SCI might take to support biotechnology research capacity strengthening in developing countries, the survey asked grantees for their opinion on establishing regional biotechnology centers. 90% of developing country respondents approved of building regional centers primarily to provide biotechnology training, technology transfer and to house specific scientific equipment. Some strongly negative comments were also elicited indicating such centers would increase bureaucracy, become too political or not be cost effective. During the site visits, the possibility of developing the capacity to supply biotechnology reagents via such centers was endorsed in discussions with several investigators.

5. SPECIAL SAFETY CONCERNS

The survey (appended) also attempted to learn how safety issues are dealt with in developing country institutions. AID/SCI currently requires documentation of adherence to U.S. standards of use of human subjects, laboratory animals, recombinant DNA and hazardous substances in provisos for approved PSTC proposals. The lack of a similar regulatory atmosphere in many countries makes the implementation of these research policies difficult.

Almost all health biotechnology projects involve one or more of these categories of concern, most commonly with infectious organisms and laboratory animals. Many involve human subjects, although usually only to provide blood samples. But some projects involved invasive procedures such as onchocerciasis nodulectomies, the induction of skin blisters in leprosy infected tissues and leishmanial lesion biopsies require clinical skills and increase the potential for problematic secondary infections in research subjects. Ethically, treatment of disease should accompany the collection of infected patient samples. The types of recombinant DNA research found in the health biotechnology projects are currently classified in the lowest categories of concern according to the NIH guidelines, requiring only basic microbiological precautions. According to the survey, most institutions provide for some forms of safety enforcement, typically a review committee or institutional guidelines. Only two investigators working on projects involving potentially safety concerns did not report institutional regulation of some kind. The site visits provided more insight into the implementation problems raised by these issues. Animal facilities are costly and were often inadequate to insure the success of the research using infected animal models of disease. Adequate safety precautions appeared to be taken for the use and storage of radioactive materials but due to the lack of national policy in all the countries visited, disposal of long lived isotopes usually involved dilution down the sink. Short lived isotopes were stored until decay occurred. No handling procedures or human subject participation was actually observed during the site visits.

D. ADMINISTRATIVE SUPPORT OF PROJECTS BY AID/SCI

1. AID/SCI'S ROLE

AID/SCI primarily allocates staff time and effort to scientific peer review and agency consideration of proposals. AID/SCI is also empowered to serve in several supportive roles to help insure the success of the funded PSTC projects. Due to the burden of the grant making process, many of the supportive activities have been formally delegated to project officers in other A.I.D. sectors or to the A.I.D. missions in the project countries. Delegation is assumed to serve as a means of integrating PSTC research into other A.I.D. developmental

activities and "contaminating A.I.D. staff with science" (Dr. Howard Minners). Informally, the AID/SCI staff often take responsibility for helping investigators when requested. The major mechanism for following projects is biannual progress reporting by the investigators. Infrequently, site visits or investigator visits to Washington have supplemented AID/SCI's knowledge of the projects. The peer review panels pointed out several instances where technical advisory intervention during the lifespan of the health biotechnology grants would have influenced the success of the work. AID/SCI has recognized over time that their supportive activities have become limited by their increased grant processing activity and that A.I.D. project officers are often too busy or not equipped to technically assist scientific research projects. In joining forces with NAS/BOSTID this year, AID/SCI hopes to amplify considerably technical advising, monitoring, evaluation, training and networking activities in PSTC.

Delays in funding were the major criticism of AID/SCI handling of PSTC grants that emerged from comments of the peer reviewers and U.S. and developing country grantees in the survey and site visit discussions. They felt they were not well informed about the funding status of their proposals or the schedule of funding steps which occurred in the process. AID/SCI estimates that it takes an average of eighteen months to fund a preproposal approved at all stages. The PSTC review process follows a fairly consistent schedule from year to year. Approximately 500 proproposals due February 1 are processed and reviewed by AID/SCI through March, then evaluated by A.I.D. Sector Councils in April and May. Letters asking for the submission of approximately 150 full proposals are sent at the end of May. The full proposals received by the September 15 deadline are peer reviewed in October. Approval letters are issued at the end of November. After review, many administrative steps are taken before funds are obligated. The investigators must respond to the reviewers' provisos and AID/SCI must receive A.I.D. mission and S&T Bureau approvals before authorization to issue a grant can be obtained. The earliest completion of these steps usually occurs in March and the latest in September at the end of the fiscal year when all AID/SCI obligations must be completed. The investigators seem most confused by the gap in time from hearing that their proposal was approved in November and not receiving word of funds for another six to nine months. For many developing country scientists the delay was even longer because funds were obligated to the U.S. institution which in turn issued subcontracts to their institution. When another six to twelve months is added to the delay in start up due to purchasing equipment and supplies to set up the laboratory, typically developing country scientists are realizing up to a three year lag from the time they submit their ideas to AID/SCI until the time they begin their research.

Another AID/SCI administrative policy has influenced start-up delays in recent years. Many more proposals have been approved

for funding than the AID/SCI budget permitted funding. AID/SCI usually holds these proposals hoping to fund them in the next fiscal year. In 1988, more than half the proposals funded were submitted to previous grant cycles as far back as the 1983-4 review. In addition to the administrative headaches imposed by funding delays, in the rapidly evolving field of biotechnology such delays may seriously compromise the quality of the research.

2. AID/WASHINGTON PROJECT OFFICERS

Approximately 50% of the health biotechnology grants are assigned to project officers in AID/Washington (table 19). Three-fourths of these are handled by S&T/Health. Half of these projects were monitored by a project officer from the Malaria Vaccine Program and another one-third by a project officer from Vector Borne Disease Control who were not available for comment. According to AID/SCI records and S&T/Health, it was unclear who took responsibility for these grants in their absence. The files contain no project officer reports. S&T/Health staff generally convey the impression that they are overburdened with their own work and PSTC projects are given low priority. S&T/Agriculture project officers for the small number of animal health projects evaluated appeared to be more receptive to PSTC and informed as to the progress in their projects.

3. MISSION PROJECT OFFICERS

Two-thirds of the health biotechnology projects assigned to missions are in Peru or Thailand. Typically, there is one person in the mission, usually the health or agriculture project officer, in charge of handling all AID/SCI grants regardless of their scientific content. AID/SCI does not maintain a formal list of the mission project officers assigned to PSTC grants in the A.I.D. Missions. The initial predominance of health or agriculturally related projects tends to determine the type of project officer assigned. But one mission, which has expressed minimal interest in the program, has assigned a specialist in fisheries to a primarily agricultural and health PSTC portfolio (Asian Trip Report). At the other extreme, the mission in Thailand has been extremely successful in utilizing PSTC as part of its science and technology mandate. The Thai mission has a science and technology division which has handled more than sixty AID/SCI grants. Robert Barnes, Dr. Gordon Hiebert and Dr. Jaroon Kumnuanta carefully monitor the projects, visiting each one quarterly in addition to organizing grant writing workshops and investigator networking meetings. An agriculture project officer handles the health projects in one mission which has caused a certain amount of confusion among the investigators there. In two other missions, health officers with a particular interest in health research have fought to give PSTC grants attention in their missions. However, both will be reassigned to new posts this year. PSTC has also been the victim of the short term assignments of A.I.D. foreign service officers in another

mission where the health, agriculture and environment officers were all new within the last year and no one knew about PSTC or the two projects in that country.

The mission project officers interviewed during each site visit (see trip reports) commented that PSTC was a way to promote science and technology for development, a way to stop the "brain drain" of researchers from national institutions and a way to maintain mission contact with the academic institutions in their country. But there were strong complaints about the management burden imposed by handling PSTC projects. They thought that the management time required for a single PSTC project was equivilent to that required for much larger projects. The mission is not compensated by AID/SCI for managing PSTC projects. The project officers are, by their own account, generally unprepared to deal with the technical aspects of research in the projects and therefore, find it difficult to write the grant agreements, review progress reports, etc., when monitoring the projects. Many said they just keep track of the financial reporting. They complained that AID/SCI did not provide adequate technical and evaluation assistance and was not sufficiently communicative about the status of funding for projects and the success of projects. Many of the approved biotechnology projects were seen by the project officers as "too high tech" or "too long range" to have an impact on development and, therefore, seemed peripheral to the health goals of the missions who were usually concentrating their efforts on maternal and child health. Of the Health Biotechnology projects visited, only in a Peruvian grant involving PRISMA, a primary health care project collaborating with diarrheal disease researchers at a local university, was the integration of PSTC and the mission health program apparent.

The survey asked the grantees about the amount of interaction they had during all stages of the PSTC granting process with AID/SCI or the A.I.D. Mission. On average, U.S. and developing country respondents reported contacting A.I.D. six times, primarily by letter. Two to three times as many contacts were reported for stages before the grant was funded. Surprisingly, both U.S. and developing country scientists reported contacting AID/SCI and the A.I.D. Mission approximately equally. Generally, the bureaucratic relationships between the A.I.D. mission, S&T/Health and AID/SCI were not clear to PSTC grantees in discussions which may invalidate their response to this question.

4. PROGRESS REPORTING

At the beginning of the evaluation, investigators were contacted regarding many progress reports missing from the files. In most cases, copies were sent to AID/SCI indicating they had regularly submitted reports to A.I.D. which apparently were either lost in the mail or not transferred to AID/SCI from mission or AID/Washington project officers. Table 17 shows that approximately 50% submitted biannual reports as required.

Another 20% submitted annual reports, many of whom were U.S. investigators possibly conditioned by the annual reporting required by NIH grants. Only 50% of the completed projects submitted final comprehensive reports but 83% of the completed projects were judged to have sufficient accumulated progress reports to permit thorough scientific peer review. Four completed project files did not contain enough reporting for review. AID/SCI prescribes no format for progress reports. The reports range from a descriptive letter to massive collections of raw data neither of which are useful for effective monitoring of scientific progress in a project (Scientific Peer Review Reports).

5. EXTENSIONS

Granting extensions requested for the two to three year PSTC projects has become routine in AID/SCI. Approximately half of the health biotechnology projects received extensions (table 18). Eighty percent (80%) of the no-cost extensions were requested for a year or less usually due to delays in receiving equipment and setting up the lab in developing countries or to finish work and data analysis to compose the final report. Four projects have received long extensions due to extenuating circumstances. No official AID/SCI mechanism or form exists for requesting an extension. In light of the large number of extension requests, AID/SCI revised the preproposal guidelines for the 1989 deadline to indicate that project duration should be 4-5 years instead of 2-3 years.

V. SUMMARY AND RECOMMENDATIONS OF PSTC HEALTH BIOTECHNOLOGY EVALUATION

Almost all scientists contacted during the evaluation were in agreement that PSTC offers a unique opportunity for collaborative research in health biotechnology. Developing country scientists tend to view PSTC as a means for training and technology transfer whereas U.S. scientists tend to view PSTC as adding a field study dimension to their laboratory based studies on tropical disease. Overall, the previous analysis demonstrates that PSTC health biotechnology projects have produced state-of-the-art research resulting in internationally read publications and examples of subsequent funding opportunities. Indirectly, PSTC health biotechnology grants have contributed to research institutition strengthening and potentially produced new tools in the struggle against tropical disease. The following commentary represents assessments and recommendations for specific issues addressed in the evaluation.

A. SCIENTIFIC SUCCESS

Post facto, scientific peer reviewers judged that the majority of the health biotechnology projects achieved a significant degree of success in meeting their objectives. They thought that the projects contribute to the present level of scientific progress

in tropical disease and no project failed due to a lack of perceived scientific merit. As indicated by the previous analysis, it appears that the health biotechnology proposals reviewed by AID/SCI may generally be superior in quality to proposals in other PSTC categories. AID/SCI's subsequent success in health biotechnology may reflect this difference in its chosen portfolio.

AID/SCI has questioned whether the criteria of high scientific merit and innovation are compromised by enforcing the criteria of relevance to international development and developing country scientific capacity strengthening. The results of the peer review of completed projects would argue that compromise is not required. The most scientifically successful projects were also rated high in benefit to international development and capacity stengthening if they initially included substantial developing country collaboration. Likewise, most scientifically unsuccessful projects ranked lowest in their contribution to development. But this judgement is based on the judgement initially made to approve these projects in which AID/SCI aimed to balance the degree of predictable scientific success and innovation with the potential for developmental benefit. From a purely scientific viewpoint, it appears that PSTC did not fund projects with a high potential for conceptual or technological breakthroughs. But AID/SCI did fund scientists to utilize technical scientific advances in biotechnology for new approaches to tropical disease. From a purely developmental viewpoint, PSTC did not fund projects with a high potential to make immediate, significant impacts on developing country health. But several of the projects produced "products" that are ready to take subsequent steps toward applications which conceivably will change tropical public health efforts in the near future. The key to PSTC's success is promoting the <u>potential</u> of scientific advances in biotechnology to provide <u>potential</u> solutions to developing health problems via taking the research steps towards new diagnostics, chemotherapeutics and vaccines. The impact of PSTC research on health in developing countries awaits a long range evaluation.

Publication is often used as a specific measure of scientific success. The majority of the projects reported producing publications, mostly in international scientific journals. But twice as many exclusively U.S. authored publications were reported. A multitude of reasons could be invoked to explain this result. This evaluation did not document the causes of lower developing country authorship. Regardless, AID/SCI should consider steps to insure developing country scientist participation in the scientific literature for their mutual benefit and to achieve AID/SCI's objective of disseminating research results to advance worldwide tropical disease efforts.

Another indicator of scientific success is the ability to obtain subsequent research funding. For many develping country

scientists a PSTC grant provides the startup funds to initiate biotechnology research. A PSTC grant, in monetary terms and time frame, is adequate to set up a sustainable biotechnology laboratory to accomplish a discreetly planned project. Much of biotechnology experimental work depends on comparatively expensive, labile reagents and disposable supplies as opposed to large equipment. Therefore, continued progress requires supplemental funding. PSTC participants report being most successful at acquiring follow-on PSTC grants and some have gone on to receive substantial grants from other sources. PSTC can breed additional opportunities for funding and AID/SCI may wish to encourage follow-on funding attempts in PSTC or other grant programs in order to sustain the efforts they initiate.

Follow-on support is especially critical for projects that have produced products ready to begin field testing and other steps towards application. Ten health biotechnology projects appear to have produced potential applications, mostly diagnostic tools. Currently, PSTC's proposal topic limitations virtually exclude funding field work. Other S&T/Health programs have not "picked up" these projects for further development as initially envisioned by AID/SCI. AID/SCI is anxious to see their research successes move towards fruitful application and is now considering how they might pursue new approaches to follow-on activities. AID/SCI may wish to consider a specific grant extension process for projects that reach this stage to take advantage of the ongoing laboratory effort to support field testing. Developing country scientists often have established access to patients and experience in health field research which would provide the appropriate setting for field tests. Ongoing A.I.D. Mission and national health programs may provide opportunities for integration with PSTC research projects at this stage.

A small number of biotechnology companies are moving into producing diagnostics and vaccines for tropical diseases. In somewhat of a precedent, WHO/TDR recently has played an intermediary role in interfacing their research efforts with industrial development of new applications to meet specific tropical public health needs. For example, WHO/TDR coordinated ivermectin field trials for onchocerciasis for Merck Corporation who has agreed to provide the drug free to all those in need in developing countries. The Office of Technology Assessment[3/], after reviewing current research for tropical disease, recommended that Congress encourage A.I.D. to interest private companies in developing medical technologies for tropical diseases by guaranteeing the purchase of products and assisting in field trials.

3/ Status of Biomedical Research and Related Technology for Tropical Diseases, U.S. Congress, Office of Technology Assessment, U.S. Government Printing Office, September 1985

B. AREAS OF RESEARCH

The portfolio of the health biotechnology projects closely resembles the tropical disease priorities determined by WHO/TDR[4/]. But the Biotechnology/Immunology module was originally designed to promote technological objectives, i.e, to use new immunological biotechnology approaches to produce vaccines, diagnostic tools and immunotherapeutic agents for tropical human and animal diseases. The PSTC health biotechnology projects are only partially addressing the priority diseases recommended by the National Academy of Sciences as approachable by this technology.[2/]

Half of the health projects involve immunological technology. The others involve genetic engineering, pharmacology or basic biological studies. AID/SCI should consider broadening the title and description to Human and Animal Health Biotechnology to match the description of the portfolio of funded grants. Half of the projects are designed to produce diagnostic tools while few are targetting new vaccine candidates. This is probably due to the short term funding of the grants where successful achievement of a diagnostic monoclonal antibody or DNA probe is more reasonably guaranteed. Vaccine development, especially for complex human parasitic diseases, requires a long term, multifaceted investment. As yet, little is understood about the mechanisms of pathology or the immune response of the host for many of the tropical disease agents which impedes rationale drug or vaccine design. At this time many lines of biotechnology research are primarily permitting a great deal to be learned about these diseases and only secondarily producing medical applications. But some of the promise of biotechnology research is being realized. Biotechnology based diagnostics are now being marketed and genetically engineered vaccines are now undergoing human trials. Immunotherapeutic agents such as interferon, interleukin or specific antibody directed toxins remain experimental and medically controversial.

As detailed in the previous analysis, in spite of the involvement of S&T/Health in project selection and management, the PSTC

2/ Priorities in Biotechnology Research for International Development, proceedings of a workshop, July 26-30, 1982, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1982

4/ Tropical Disease Research, a Global Partnership at Work: New Approaches to Research Capacity Strengthening, UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases, First Edition, 1988

projects share common research goals with projects funded by S&T/Health. Both Diatech and the Malaria Vaccine Program almost exclusively fund U.S. investigators whereas PSTC uniquely aims to strengthen the scientific capacity of developing country institutions by funding research there. The Malaria Vaccine Program is narrowly defined and could be synergized by AID/SCI research in chemotherapy and mosquito vectors. For example, AID/SCI funded two projects in Papua New Guinea (on the effect of immunity on malaria transmission by mosquitos and the genetics of malarial drug resistance) which should provide valuable data for the upcoming malaria field trials there. On the other hand, PSTC funded a study of malaria antigenic variation in Thailand similar to studies funded in the S&T/Health malaria vaccine projects. The work has recently been completed but will be difficult to publish because others have published their studies already. A great deal of commonality is seen between the diagnostic tool development funded by Diatech and PSTC. Diatech has not "picked up" diagnostic projects initially funded by AID/SCI. AID/SCI should work with S&T/Health to define these funding efforts in order to insure complementarity and non-overlapping objectives.

Only a handful of veterinary projects have been supported under the auspices of the Biotechnology/Immunology module despite high priority recommendations for animal vaccines and diagnostics by the National Academy of Sciences. In many ways, more success might be achieved in a shorter time frame in applying the new immunological biotechnology approaches to veterinary disease. The efficacy and safety requirements for animal vaccines are quite different than for human vaccines. For example, vaccinia virus engineered to carry vaccinating proteins provides many of the desirable characteristics, e.g., heat stability, easy one time inoculation, simple production, high likelihood of correct expression and presentation of antigen to the immune system, capacity of expressing multiple vaccine candidates. Unfortunately, vaccina virus based vaccines may have limited utility for human use because of their use in smallpox irradication and the potential side effects elicited in immunosuppressed individuals. But vaccinia based vaccines may have great potential for veterinary vaccines where these effects are not relevant. Veterinary research is generally undersupported by the major donors. S&T/Agriculture is actively pursuing biotechnology approaches for rinderpest, anaplasmosis and babesiosis vaccines and may be receptive to complementary PSTC supported research or initiatives in other diseases. AID/SCI may consider reorienting their health biotechnology efforts to include more emphasis on tropical veterinary diseases.

C. U.S.-DEVELOPING COUNTRY COLLABORATION

Collaboration between U.S. and developing country scientists is the cornerstone to fulfilling the PSTC mandate. In a sense, it is the most pliant element in the projects. Scientific merit, technical innovation and relevance to development are all

inherent in the substance of the proposals. AID/SCI is most able to intervene during the grant approval process to encourage stronger capacity strenthening by requiring that more budget, more project responsibility, more training or more interaction involving travel be included for developing country participants. These indicators were examined in the funded health proposals along with subjective evaluations from the grantees and from the peer review scientists.

The total distribution of PSTC funds for health biotechnology grants is almost equal between U.S. and developing country participants but few projects result in equal financial sharing. The analysis of various indicators of collaboration showed that the U.S. collaborators dominate in the majority of the health biotechnology project relationships. AID/SCI may have reason to be concerned with the number of Washington area investigators receiving these grants. Overall, the health projects involved some of the most highly regarded U.S. and developing country tropical disease researchers and institutions.

The health biotechnology projects are distributed worldwide in comparative proportions to other PSTC grants. The level of participation indicates that scientists from more advanced developing countries may be more institutionally capable and eager to engage in this relatively more basic and intensely technical research category of PSTC than many of the less advanced countries, especially in Africa, which are not as well represented in the program. AID/SCI may need to make special efforts to engage in health biotechnology research in these countries, possibly by broadening the scope of research to include more epidemiology and applied field research for which there is usually more demand and more scientific strength in these countries. In addition, AID/SCI may wish to consider new mechanisms to encourage and support collaborations between the excellent tropical disease research institutions in advanced developing countries in need of research funds and neighboring, less advanced countries with similar health problems. The projects stand to gain as much or more from collaborations with advanced developing country scientists, often with both laboratory and field experience, than from U.S. collaborators.

The U.S. collaborative role in the health biotechnology projects ranges from acting as an expert consultant, to providing technical or advanced degree-related training, to working for substantial periods in the developing country laboratory, to directing the project in the U.S. which receives or collects samples in a developing country. All levels of collaboration were found in successful projects although projects with minimal developing country participation or U.S. participation were the most problematic. AID/SCI policy changed early in the program to require developing country participation but even between 1984 and 1986 seven health biotechnology projects were funded that devoted less than 10% of their budget to the developing country

participants. In many instances, AID/SCI encounters more bureaucratic barriers in funding projects through developing country institutions. Specific efforts and strategies are needed to overcome these barriers. The peer reviewers were also critical of exclusively developing country projects indicating the probable need for a technical "fairy godmother/father" to be involved in guiding, supplementing and trouble shooting at critical junctures in the research. AID/SCI needs to develop and enforce a more consistent definition of collaboration in the PSTC projects, possibly by requiring a commitment to a defined work schedule and division of labor in the proposals and requiring progress reporting on collaborative interactions.

From the developing country scientists' viewpoint, training was the most effective and sought after element of their PSTC experience and most often formed the basis of collaboration. Difficulties in communication were the most frequent complaints about collaboration. AID/SCI, via a new cooperative agreement with BOSTID/NAS, is considering many ways to enhance networking and training possibilities for PSTC grantees.

D. CAPACITY STRENGTHENING

The PSTC health biotechnology grants enhanced many other components, in addition to training, that increased scientific capacity in the developing country laboratories funded. Most of the equipment purchased with these grants was incorporated into developing country laboratories. The funding for many projects allowed the investigators to equip and supply their laboratory to engage in biotechnology research on par with many U.S. labs. Unfortunately, due to a variety of problems in ordering, shipping, currency exchange, etc., involved in purchasing equipment and supplies the initiation of the research project was often delayed up to a year. These delays were the major reason for requests for grant extensions. Some A.I.D. missions assisted with customs and currency exchange problems in their countries. Their methods could be useful to other mission project officers handling PSTC grants and should be included in the forthcoming PSTC Project Officer's Handbook. AID/SCI might consider giving developing country investigators the option of withholding the equipment and supply portion of their grant in a U.S. account (for U.S. purchasing) and assisting in the ordering and shipping process in order to circumvent start-up delays.

It is clear from the level of developing country participation in publishing the results of the projects that the deficiencies exist in the capacity for developing country grantees to use and contribute to the scientific literature. AID/SCI should encourage developing country PSTC grantees to use a small portion of their funds (less than 5%) for bibliographic and publication services, e.g., journal subscriptions, abstract listings, photographic equipment, computer software, copying. WHO/TDR provides extensive tropical disease reports and publication

listings and all health biotechnology grantees could easily be added to their mailing lists. The technical "fairy godmother/father" might play a role in passing on appropriate references, technical protocols or announcements of scientific meetings or workshops. AID/SCI should consider offering investigators the option of asking for assistance (editing, graphics, etc.) in publishing their work. The scientific reputation of PSTC could only be enhanced by greater sponsorship of scientific publication.

Increased administrative capacity was not generally perceived by the grantees to be a result of PSTC funding. The previous analysis indicates there are additional barriers to getting grants operating in developing country institutions. AID/SCI may wish to evaluate the reasons for these barriers or ways to surmount them possibly using the overhead funds available from the grants. In addition, AID/SCI may be able to assist developing country institutions in setting up safety standards and practices, ethical committees and monitoring systems for areas of special regulatory concern (human subjects, experimental animals, recombinant DNA, infectious organisms, radioactive materials, toxic chemicals) inherent in biotechnology health research.

Qualitatively, PSTC biotechnology projects in developing countries have had an impact on the direction of research at some of the institutions involved. The PSTC projects have demonstrated that the technology is approachable and readily successful. This seems to have convinced some administrators of the promise of biotechnology for health research in developing countries and given them confidence in expanding their efforts in this direction.

E. ADMINISTRATIVE SUPPORT OF PROJECTS BY AID/SCI

AID/SCI has focussed its time and efforts on the grant making process. Supportive activities have been largely delegated to A.I.D. Project Officers in Washington and in the missions. Often there was good U.S. collaboration, strong developing country scientific involvement and a host of other favorable factors and many of the health biotechnology projects were successful at meeting their objectives after receiving funds with little A.I.D. involvement. But a greater commitment to in-depth, ongoing technical monitoring and evaluation might have enabled many of the projects to be even more successful.

The new cooperative agreement with NAS/BOSTID offers new opportunities for providing PSTC grantees scientific advisory and technical problem solving support which could well have great impact especially on developing country scientists. In an effort to standardize, inform and make monitoring and evaluation efforts more effective, handbooks detailing procedures, responsibilities and support services available are now being written for PSTC

grantees and project officers. NAS/BOSTID will regularly communicate with grantees about their scientific progress, offer networking possibilities, technical workshops, references and other services which should greatly enhance the projects and support the administrative efforts of A.I.D. project officers.

A.I.D. missions, especially those with multiple PSTC grants, would like to see more benefit in the projects when weighed against their management burden. AID/SCI should consider contributing some funds to missions for administrative costs. These funds could possibly be used to hire national scientists for administering the projects (patterned on the success of Dr. Jaroon in Thailand). Such local scientific administrative assistance could provide the continuity and expertise for mission personnel dealing with PSTC research projects as well as supporting the grantees and providing a vital link for NAS/BOSTID and AID/Washington support personnel.

The A.I.D. mission may also see more benefits from the health biotechnology research projects if more effort could be made to integrate the projects with mission human and animal health programs. Meetings could be sponsored between national health or veterinary researchers and practitioners in these fields to discuss new techniques becoming available for diagnosis, epidemiological work, etc.

For projects with successful "products" AID/SCI and mission jointly sponsored follow-on field testing studies could be envisioned which take advantage of the local scientific efforts in conjunction with local health care programs. S&T/Health and health biotechnology company collaboration could also be included. With many health biotechnology projects successfully reaching completion, it is timely to consider how to promote their contributions to the arduous task of improving health care in developing countries. Forming the difficult link between local biotechnology research and application represents one of the largest barriers to sustainable technological development (PSTC Conference on Biotechnology for Health and Agriculture Abstracts).

REFERENCES

1/ The U.S. Capacity to Address Tropical Infectious Disease Problems, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1987

2/ Priorities in Biotechnology Research for International Development, proceedings of a workshop, July 26-30, 1982, Board on Science and Technology for International Development, Office of International Affairs, National Research Council and Institute of Medicine, National Academy of Sciences, National Academy Press, Washington, D.C., 1982

3/ Status of Biomedical Research and Related Technology for Tropical Diseases, U.S. Congress, Office of Technology Assessment, U.S. Government Printing Office, September 1985

4/ Tropical Disease Research, a Global Partnership at Work: New Approaches to Research Capacity Strengthening, UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases, First Edition, 1988

5/ Purchase, Use and Maintenance of Scientific Equipment in Developing Countries, J.F. Gallard and S. Quatter, Interciencia, Vol 13, No. 2, March-April 1988

TABLE 1: PSTC HEALTH BIOTECHNOLOGY GRANTS REVIEWED AND METHODS OF EVALUATION

The PSTC projects included in the evaluation of health biotechnology are listed with the location of their collaborators. Evaluation methods included site visits described in trip reports, scientific peer review conference presentations and survey replies (individual project reports for each of these methods are appended).

(1) Site visits were conducted by:

- (BS) - Dr. Barbara Sina (AAAS Fellow AID/SCI)
- (JR) - Dr. Janet Rice (AAAS Fellow ANE/TR)
- (EB) - Dr. Elizabeth Beckmeyer (AAAS Fellow S&T/H)
- (CS) - Dr. Clive Shiff (S&T/H)
- (KS) - Dr. Kathy Satterson (ANE/PD/ENV)
- (PI or CoPI) - Principal or co-investigator conversation instead of a site visit

(2) (*) Follow-on PSTC proposals were submitted and evaluated by scientific peer review.

(3) Projects not designated in the Biotechnology/Immunology module

1404b

Table 1A: PSTC HEALTH BIOTECHNOLOGY GRANTS REVIEWED AND METHODS OF EVALUATION

Project Number	Title	Principal Investigator	Co-Principal Investigator	Evaluation Methods: Trip Report[1]	Peer Review	Conference Presentation	Survey Returned
1H02	Immunization against Trypanasomiasis: Non-glycoprotein Surface Component Approach	Univ California-San Diego	Kenya-British	BS	*[2]		
2H01	Antimalarials Selectively Toxic to the Parasite[3]	USUHS	None	PI	X		X
2H08	Specific Circulating Antigens in Malaria and Schistosomiasis	USUHS	Zambia	PI			
2H12	Production of Shiga-like Toxin by E. coli[3]	USUHS	None		X		
2H13	Pathogenesis of Viral Diarrhea: Toxin Recognition Approach	USUHS	None		X		
2H14	Purification of Mycobacterial Antigens for Use in Serological Diagnosis of Tuberculosis	East. Va. Medical School	India		X		
3F04	Control of Tick Transmitted Diseases by Vaccination of the Host	Ohio State Univ.	Domican Republic		*	X	X
3F31	Production of Antigens of Onchocera Volvulus by Recombinant Microbiology	John Hopkins	Cameroon	BS	X		
3F33	New Approaches to Control of Bovine Babesiosis	Univ Missouri	Mexico		X*	X	
3F34	Transmission Blocking Immunity and Infectivity of Human Populations to Mosquitos during Malaria Transmission	Papau New Guinea (Australians and British)	NIH	PI			
3F54	Development of Monoclonal Antibodies Against Trypanasoma Cruzi	Venezuela	Harvard		X		
3H09	Effect of Chemotherapeutic Agents on Malaria Sporozoites In Vitro[3]	Rutgers	None		X	X	

Table 1A: PSTC HEALTH BIOTECHNOLOGY GRANTS REVIEWED AND METHODS OF EVALUATION

Project Number	Title	Principal Investigator	Co-Principal Investigator	Evaluation Methods: Trip Report	Peer Review	Conference Presentation	Survey Returned
3H18	ELISA Diagnosis of Tuberculosis in Bolivia	Case Western Res.	Bolivia	BS/PI	X		X
3H22	Cicatrizant Properties of the Plant Extract Sangre de Grado[3]	Peru	None	BS	*	X	
3H24	Development of ELISA for Immunodiagnosis of Onchocerciasis	Johns Hopkins	Cameroon	BS	X	X	
3H33	Comparison of Two In Vitro Techniques for Culture of Plasmodium falciparum	Thailand	PC Volunteer	JR	X		
4.178	Environmental Microbiology Studies in Bangladesh	Univ Maryland	Bangladesh	PI	X	X	X
4.227	Immunology of Amebiasis	Mexico	None		*		
4.321	Studies on Parasite-Vector Relationships in Leishmaniasis	Israel	Egypt		X		
4.348	Detection of Snails Infected with Schistosoma mansoni Using Molecular Probes	Israel	Kenya	BS	*	X	
4.410	Microbial Genetics Study of Transmission and Pathogenesis of Infantile Diarrhea	Johns Hopkins	Burma			X	X
4.468	Speciation of Infective Larvae of Filaria and Identification of Species Specific Antigens of Brugia malayi	Harvard	Indonesia	JR			
4.528	Improvement of Bacterial Agents for Control of Mosquito Vectors[3]	Thailand	None	JR		X	X
4.577	Proteolytic Enzymes of Fasciola hepatica as markers of Human and Animal Infection	Peru	Baylor	BS	X*	X	X

Table 1A: PSTC HEALTH BIOTECHNOLOGY GRANTS REVIEWED AND METHODS OF EVALUATION

Project Number	Title	Principal Investigator	Co-Principal Investigator	Evaluation Methods: Trip Report	Peer Review	Conference Presentation	Survey Returned
4.607	T. ferroxidans Strains Resistant to High Metal Concentrations	Peru	Ohio State	BS		X	X
4.633	Chloroquine and Quinine Receptors in Plasmodium falciparum[3]	Univ New Mexico	None		X		
5.002	Development of Vaccine Against Severe Hepatosplenic Disease in Schistomiasis japonica	Philippines	Australia	EB	X	X	
5.038	Epidemiology of Mokolo Virus Infection	Zimbabwe	CDC	CS			X
5.052	Expression of Mosquito Toxin Gene of Bacillus thuringensis in Cyanobacteria[3]	Univ Wyoming	India	PI		X	
5.130	Genetics of Parasite Populations involved in Transmission of Human Schistosomiasis	Brazil	NIH	BS CoPI		X	X
5.140	In Vitro Evaluation of Interleukins 1 and 2 as Immunotherapeutic Agents for Leprosy	Thailand	Univ Hawaii	JR	X	X	X
5.141	Immunoperoxidase Test for Early Diagnosis of Acute Reactional States in Leprosy Patients	Thailand	Univ Hawaii	JR	X	X	X
5.148	Immunological Response to Schistosoma mansoni in Occupationally Exposed Workers	Sudan	Michigan State		X		X
5.189	Immunogenic Proteins of Onchocerca volvulus Adult Worms, Microfilariae & Larvae	Sierra Leone	Case Western	CoPI			
5.203	Diagnosis of Human Leishmaniasis Using Biotinylated K-DNA Probes	Peru	Harvard	BS	X	X	X
5.221	Immunodiagnosis and Improvement of Immunotherapy of Snake Venom Poisoning	Thailand	US Visiting Scientist	JR		X	

Table 1A: PSTC HEALTH BIOTECHNOLOGY GRANTS REVIEWED AND METHODS OF EVALUATION

Project Number	Title	Principal Investigator	Co-Principal Investigator	Evaluation Methods: Trip Report	Peer Review	Conference Presentation	Survey Returned
5.224	Immunodiagnosis and Immunoregulation in Tuberculosis	Thailand	None	JR	X		X
5.227	Production of Monoclonal Antibodies to Salmanella Species	Thailand	Univ Alabama	JR		X	X
5.232	Antigenic Diversity of *Plasmodium vivax*	Thailand	None	JR		X	
6.132	Monoclonal Antibodies for Immunodiagnosis of of Hydatid Cyst and Echinococcus Antigen	Jordan	None	KS		X	X
6.225	Immunogenic Proteins of Microfilaria and Adult Worms of *Onchocerca volvulus*	Guatemala	CDC			X	X
6.299	Gene Probes for Rapid Detection of Enteric Viruses in Water and Sewage	Univ Arizona	Bolivia	BS		X	X
6.317	Polyamine Synthesis Inhibition as Therapy for *Trypanosoma Rhodesiense Infection*	Kenya	NYU	BS CoPI		X	
6.345	Traditional Peruvian Remedies for Diarrheal and Parasitic Infections[3]	Peru	Johns Hopkins	BS			
6.390	Cloning of Surface Antigen Genes of Schistosoma japonica	Thailand	None	JR			
6.391	Immunopathogenesis of Dengue Hemorrhagic Fever and Shock Syndrome	Thailand	None	JR			
6.392	Methods for Immunodiagnosis of Human Liver Fluke Infection	Thailand	None	JR		X	
6.419	Monoclonal Antibodies Against Entamoeba histolytica	Thailand	None	JR		X	

TABLE 1B: SUMMARY OF METHODS OF EVALUATION

Method	Number of Projects	% Projects
Site Visits	34	70.8
Peer Review	21	43.8
Follow-on PSTC Proposal	7	14.6
Conference Presentation	26	54.2
Survey	19	39.6
Projects Evaluated by:		
1 method	13	27.1
2 methods	15	31.3
3 methods	14	29.2
4 methods	5	10.4

1406b

TABLE 2: COMPARISON OF THE NUMBER OF BIOTECHNOLOGY/IMMUNOLOGY PREPROPOSALS AND GRANTS TO OTHER MODULES

(A) % Preproposals Funded for PSTC Modules
(B) % Total Preproposals Submitted for PSTC Modules
(C) % Total Funded Grants for PSTC Modules

Modules:

BIOT/I - Biotechnology/Immunology
BIOT/P - Plant Biotechnology
CHEM - Chemistry for World Food Needs
VECT - Biological Control of Human Disease Vectors and Plant Pests and Pathogens
GEN - Diversity of Biological Resources
ENG - Engineering Technology
MAR/EAR- Marine and Earth Sciences
BMAD - Biomass Resources and Conversion Technology

TABLE 2A: COMPARISON OF THE NUMBER OF BIOTECHNOLOGY/IMMUNOLOGY PREPROPOSALS (PP) AND GRANTS TO OTHER MODULES (1982-1986)
PERCENT PREPROPOSALS (PP) FUNDED FOR PSTC MODULES

	1982			1983			1984			1985			1986		
Module	PP	Grants	% PP Funded	PP	Grants	% PP Funded	PP	Grants	% PP Funded	PP	Grants	% PP Funded	PP	Grants	% PP Funded
BIOT/I	17	3	17.6	28	5	17.8	75	12	16.0	50	14	28.0	90	16	17.8
BIOT/P	6	3	50.0	17	2	11.8	30	10	33.3	37	13	35.1	64	8	12.5
CHEM	18	4	22.2	38	9	23.7	64	5	7.8	80	6	7.5	132	10	7.6
BMAS	17	5	29.4	33	5	15.2	38	8	21.1	55	5	9.1	66	5	7.6
VECT	9	2	22.2	27	4	14.8	36	6	16.7	40	12	30.0	41	11	26.8
GEN	20	3	15.0	32	5	15.6	74	2	2.7	30	5	16.7	65	6	9.2
ENG	22	4	18.2	76	7	9.2	77	2	2.6	42	4	9.5	46	4	8.7
MAR/EAR	24	2	8.3	46	4	8.7	74	2	2.7	48	1	2.1	51	4	7.8
TOTAL	236	26	11.0	425	41	9.6	634	47	7.4	441	60	13.6	609	64	10.5

1408b

TABLE 2B: PERCENT TOTAL PREPROPOSALS SUBMITTED FOR PSTC MODULES

Year	BIOT/I	BIOT/P	CHEM	BMAS	VECT	GEN	ENG	MAR/EAR
1982	7.2	2.5	7.6	7.2	3.8	8.5	9.3	10.2
1983	6.6	4.0	8.9	7.8	6.3	7.5	17.9	10.8
1984	11.8	4.7	10.1	6.0	5.7	11.7	12.1	11.7
1985	11.3	8.4	18.1	12.5	9.1	6.8	9.5	10.9
1986	14.8	10.5	21.7	10.8	6.7	10.7	7.6	8.4
AVERAGE	10.3	6.0	13.3	8.9	6.3	10.3	11.3	12.7

TABLE 2C: PERCENT TOTAL FUNDED GRANTS FOR PSTC MODULES

Year	BIOT/I	BIOT/P	CHEM	BMAS	VECT	GEN	ENG	MAR/EAR
1982	9.1	9.1	12.1	15.2	6.1	9.1	12.1	6.1
1983	10.9	4.3	23.9	10.9	8.7	10.9	15.2	8.7
1984	23.1	19.2	9.6	15.4	11.5	3.8	3.8	3.8
1985	22.6	21.0	9.7	8.1	19.4	8.1	6.5	1.6
1986	22.5	11.3	14.1	7.0	15.5	8.5	5.6	5.6
AVERAGE	17.6	13.0	13.9	11.3	12.2	8.1	8.6	6.9

TABLE 3: THE NUMBER OF APPROVED PROPOSALS COMPARED TO FUNDED PROJECTS IN 1988

Module	Approved by 1988 Peer Review	Funded 1988	% Approved that were Funded
BIOT/I	10	3	30.0
BIOT/P	10	4	40.0
CHEM	9	5	55.5
BMAS	5	5	100.0
VECT	5	3	60.0
GEN	6	2	33.3
ENG	1	1	100.0
MAR/EAR	3	2	66.7
TOTAL	49	25	51.0

1411b

TABLE 4: REGIONAL DISTRIBUTION OF PSTC HEALTH BIOTECHNOLOGY GRANTS (1982-1986)

Year	Africa	Asia and Near East	Latin America & the Caribbean	U.S. Only
1981	1	0	0	0
1982	1	1	0	3
1983	2	2	5	1
1984	1	5	3	1
1985	3	8	2	0
1986	1	5	3	0
TOTAL	9	22	13	5
% Total Health Grants	18.8	45.8	27.1	10.4
% Total PSTC Grants	11.1	53.9	35.0	N.D.

1412b

TABLE 5: AFRICAN PARTICIPANTS IN THE XII INTERNATIONAL CONGRESS FOR TROPICAL MEDICINE AND MALARIA (AMSTERDAM, SEPTEMBER 18-23, 1988)

Benin 1
Burkina Faso 6
Cameroon 5
Central African Republic 2
Ethiopia 8
Gabon 4
Gambia 5
Ghana 2
Guinea 1
Ivory Coast 2
Kenya 24
Liberia 4
Malawi 1
Mali 1
Mozambique 2
Nigeria 41
Rwanda 1
Senegal 5
Sierra Leone 1
Somalia 3
Sudan 9
Tanzania 23
Togo 1
Uganda 4
Zaire 3
Zambia 7
Zimbabwe 15

1413b

TABLE 6: TROPICAL HUMAN AND ANIMAL DISEASE RESEARCH PROJECTS FUNDED BY PSTC

Malaria [a]	7	Tuberculosis	2
Schistosomiasis [a]	7	Trypanosomiasis [a]	2
Onchocerciasis [a]	6	Chagas Disease [a]	2
Diarrheal Disease	10	Leishmaniasis [a]	2
Viral 2		Makola Virus	1
Bacterial 5		Babesiosis	1
Protozoan 3		Echinococcus	1
Liver Fluke	4	Dengue Fever	1
Filariasis [a]	3	Leprosy [a]	2
Other	5		

[a] WHO/TDR priorities

1414b

TABLE 7: DIATECH PROJECTS FUNDED BY S&T/HEALTH

Institution	Title
Centers for Disease Control	Production and Characterization of MAbs against parainfluenza
University of Kentucky Research Foundation	ELISA for the rapid diagnosis of influenza
University of Washington	Development and testing of reagents for M. tuberculosis
Koninklijk Instituut voor de Tropen	Development of field assay for detection of M. tuberculosis
International Health Services	Sputum sampling method for diagnosis of tuberculosis
McClellan Memorial Veterans Hospital	Evaluation of DNA probes for diagnosis of tuberculosis
Minnesota Mining and Manufacturing Company	Advanced agglutination assay for S. pneumoniae
University of Rochester	Development of ELISA for rapid diagnosis of influenza
Research Foundation of SUNY	Development of Monoclonal Antibodies to Pneumococcus
Henry M. Jackson Foundation	Colony-ELISA for detection in stool of E. coli
Sero-Immuno Diagnostics, Inc.	Serological detection of G. lamblia in stool
Standford University Medical Center	Detection of EPEC with the EPEC-specific carbohydrate receptor
University of Virginia	Development of a lectin-specific ELISA for amebiasis
Dynamac Corporation	Field-suitable ELISA for detecting Salmonella Vi antigen
The Johns Hopkins University/DIID	Indium slide assay for diagnosis of typhoid fever
Land O'Lakes	Development of assays for detection of S. typhi
University of Maryland at Baltimore/CVD II	Preparation of MAb for detection of enteropathogenic E. coli
Mahidol University/Faculty of Medicine	Development of Vi Monoclonal Antibodies for Typhoid Fever
Genetic Diagnostics Corporation	Disposable Diagnostic Device for E. coli Enterotoxins
University of Virginia Dept. of Geog. Medicine	Studies of Simpler Methods of Detection of Fecal Leukocytes
Medical College of Pennsylvania	DNA Probe for Giardia lamblia
University of Maryland at Baltimore/CP	Evaluation of five probes for the diagnosis of malaria
Institute of Zoology, Zoological Society	ELISA for the measurement of plasma quinine levels
Professional Staff Association	Development of assay for detection of P. vivax DNA in blood
Georgetown University	Development of monoclonal antibody-based assay for malaria
University of Maryland at Baltimore/CVD 1	Development of ELISA for detection of P. falciparum
University of Illinois	Detection of malaria parasites using synthetic DNA probes
Mahidol University/Faculty of Tropical Medicine	Two-site ELISA for the Detection of P. falciparum Antigen
The Johns Hopkins University/Primary	Provision of assistance to management/laboratory resources
University of Maryland at Baltimore/Primary	Provision of assistance to management/laboratory resources
Miami University	Development of dilution sensors for ORS solutions
Queen Saovabha Memorial Institute/Primary	Provision of assistance to management and sample collection
The New York Blood Center	Development of O. volvulus diagnostics for third-world use
Artel, Inc.	Development of a direct-reading hemoglobinometer
University of Virginia School of Medicine	Rapid Diagnostic Tests for Detection of Visceral Leishmaniasis

TABLE 8: PRIORITIES FOR HEALTH BIOTECHNOLOGY RESEARCH (1982 NATIONAL ACADEMY OF SCIENCES WORKSHOP)

Human Diseases	Vaccines	Monoclonal Antibody Diagnostics	NAS Recommended PSTC Projects
Rabies [1]	X	X	1
Dengue Fever	X		1
Japanese Encephalitis	X		
Bacterial Respiratory Diseases			
Pneumococcus	X	X	
Pertussis	X		
H. influenzae	X	X	
Bacterial Enteric Diseases			
Campylobacter jejune	X	X	
E. coli	X	X	1
Salmonella	X	X	3
Shigella	X	X	
Vibrio cholerae	X		1
Chlamydia	X		
Malaria	X	X	4
Leishmaniasis	X		
Streptococcus		X	
Cysticercosis		X	
Ascarus		X	
Amebiasis		X	2
Echinococcosis		X	
Filariasis		X	1
Schistosomiasis		X	3
Toxaplasmosis		X	
Equine Encephalitis		X	
Tuberculosis [1]	X	X	3
German Measles		X	
Hepatitis		X	
Herpes Virus		X	
Animal Diseases			
Neonatal Diarrhea	X		
Pasteurella	X		
Bordetella	X		
African Swine Fever	X	X	
Babesiosis	X	X	1
Anaplasmosis	X	X	
Brucella		X	
Fascioliasis		X	1
Coccidiosis		X	
Atrophic Rhinitis		X	
Blue tongue		X	
Caprine Arthritis		X	
Equine Infectious Anemia		X	
Foot and Mouth Disease		X	
Bovine Rhinotracheitis		X	
Marek's Disease		X	
Newcastle's Disease		X	

(1) Zoonotic disease- priority for both human and animal hosts

TABLE 9: TECHNICAL GOALS OF PSTC HEALTH BIOTECHNOLOGY GRANTS

Immunological Biotechnology	
Vaccine	8
Diagnostic	21
Recombinant DNA Diagnostic	11
Chemotherapy	8
Basic Biology/Pathology	7
Other	3

TABLE 10: SUMMARY OF SCIENTIFIC PEER REVIEW OF COMPLETED HEALTH BIOTECHNOLOGY PROJECTS

	% PROJECTS						
Criteria	Excellent	Good to Excellent	Good	Fair to Good	Fair	Poor to Fair	Poor
Scientific Quality	9.5	14.3	52.4	0	23.8	0	0
Capacity Strengthening	9.5	14.3	23.8	4.8	19.0	0	28.6
Contribution to the Field	4.8	9.5	47.6	4.8	19.0	9.5	4.8
Benefit to Internat'l Dev.	4.8	4.8	52.4	4.8	23.8	4.8	4.8

Overall, the reviewers found the projects to be:

Successful in meeting their objectives	38.1%
Partially to fully successful	19.0
Partially successful	33.3
Unsuccessful	9.5

1418b

TABLE 11: RANKING OF PEER REVIEWED HEALTH BIOTECHNOLOGY PROJECTS

Project	Rank in Overall Success[1/]	Rank in Combined Criteria[2/]
A	1	7
B	1	1
C	1	2
D	2	3
E	3	6
F	3	8
G	3	3
H	3	3
I	4	2
J	4	9
K	4	5
L	5	9
M	6	4
N	7	12
O	7	4
P	7	10
Q	8	12
R	9	6
S	9	11
T	10	9
U	11	11

1/ Average of reviewers' ratings for success in reaching scientific objectives (see Table 10).

2/ Average of reviewers' ratings for the criteria of scientific quality, capacity strengthening, scientific contribution and benefit to international development (see Table 10)

TABLE 12: SCIENTIFIC PUBLICATIONS REPORTED BY HEALTH BIOTECHNOLOGY GRANTEES

A. Type of Publication	% Total Publications	% Publications with Developing Country Authors
Scientific Journal Article	67.2	36.6
Scientific Meeting Proceedings/ Abstracts	27.5	14.5
Review Articles/Chapters	5.3	0.8

B. Publications Per Grant	All Grants	Completed Grants
% Grants with Publications	54.2	66.7
% Grants with Developing Country Authored Publications	31.3	43.3
Publications Per Grant	2.7	4.4
Developing Country Authored Publications Per Grant	1.4	2.3
Journal Publications Per Grant	1.8	2.9
Developing Country Authored Journal Publications Per Grant	1.0	1.6

C. Authors	Number of Authors	% Total Authors
Developing Country Authors	76	35.2
Non-Developing Country Authors	140	64.8

D. Region	% Health Biotechnology Grants	% Developing Country Authored Journal Articles
Africa	19.6	8.7
Asia/Near East	45.7	47.8
Latin America/Caribbean	34.8	43.5

1 Includes journal articles published, in press or submitted (manuscript on file) where USAID support was acknowledged. Eighty-six percent (86%) of the articles were published in internationally distributed scientific journals (see appended list of publications).

TABLE 13: MULTIPLE APPLICANTS FOR PSTC HEALTH BIOTECHNOLOGY GRANTS

A. Principal Investigator	% Grants	% Completed Grants
US - one preproposal	57.1	56.3
- multiple preproposals	42.9	44.8
Developing Country		
- one preproposal	60.0	45.5
- multiple preproposals	40.0	54.5

B. Success Rate of Multiple Applicants

Principal Investigator	Number	Average Attempts	% Approved for Funding
US	9	2.8	56%
Developing Country	10	2.6	56%

C. Last Point of Approval for Multiple Users' Subsequent Applications

Principal Investigator	Submit Preproposal	AID/SCI Internal Review	AID Sector Council	Peer Review	Funds Obligated
US	25.0%	12.5%	25.0%	6.3%	31.3%
Developing Country	22.2%	22.2%[1]	5.6%	27.8%	22.2%

1 Includes 16.7% preproposals submitted and approved in the US-Israel Cooperative Development Research (CDR) Program which was discontinued before full proposals were requested.

1421b

TABLE 14: RESEARCH "PRODUCTS" OF PSTC HEALTH BIOTECHNOLOGY GRANTS

Grant Number	Research "Product"
2.H08	ELISA diagnostic test for Malaria and Schistosomiasis with portable microcomputer interfaced system
2.H12	Antibody-based diagnostic for E. coli Shiga-like toxin production in diarrheal disease
3.H22	Wound healing agent isolated from traditional plant remedy
4.178	Monoclonal antibody assay for non-culturable Vibrio cholerae found in water sources
4.348	ELISA diagnostic assay for snails infected with Schistosoma mansoni
4.607	T. ferrooxidans strains resistant to high toxic metal concentrations for metal leeching of mining wastes
5.141	Skin blister assay to determine the immune status in leprosy infected tissue
5.203	Non-radioactive DNA probe assay for Leishmania infected skin biopsy samples
6.229	DNA probe assay for detection of enteric viruses in water and sewerage
6.345	Traditional plant remedy for bacterial toxin caused diarrhea

TABLE 15: TYPES OF COLLABORATIVE RELATIONSHIPS IN PSTC HEALTH BIOTECHNOLOGY GRANTS

A. Type of Collaboration	% Proposed[1]	% Achieved[2]	Success Rate (%)[3]
LDC sends samples to U.S.	10.3	7.3	50.0
U.S. sends samples to LDC	13.8	12.2	62.5
Parallel Experimentation	5.2	2.4	33.3
LDC training in U.S.	27.6	24.4	62.5
U.S. trains LDC in LDC lab	8.6	14.6	100.0[3]
Joint field work in LDC	12.1	17.1	100.0[3]
U.S. research in LDC lab	3.4	4.9	100.0[3]
U.S. consults for LDC	19.0	17.1	63.6

B. Success of Collaboration (n=28)	%
Met Proposed Goals	61.0
Partially Met Proposed Goals	14.0
Unsuccessfully Met Proposed Goals	25.0

1/ Percent of completed projects with U.S.-developing country collaboration proposed

2/ Percent of completed projects that achieved collaboration of the type indicated

3/ Percent of individual examples of each type of collaboration proposed that it was achieved

1423b

Revised

TABLE 16: PERCENT BUDGET ALLOCATED FOR DEVELOPING COUNTRY GRANTEES

A.

% Budget for Developing Country	% Health Biotechnology Grants
0	22.9
1-9	6.3
10-19	2.1
20-29	2.1
30-39	4.2
40-49	6.3
50-59	2.1
60-69	6.3
70-79	2.1
80-89	4.2
90-99	16.7
100	25.0

B. Percent Budget Allocated for Developing Country Grantees Compared to Success Rated by Peer Review

Top Ranked[1/] in Overall Success		% Budget	Top Ranked[1/] by Combined Criteria		% Budget
1.	A	0	1.	B	0
	B	0	2.	I	0
	C	100.0		C	100.0
2.	D	44.4	3.	G	40.6
3.	E	0		D	44.4
	F	0		H	93.8
	G	40.6	4.	O	24.4
	H	93.8		M	36.6

1/ See Tables 10 and 11

TABLE 17: BUDGET ALLOCATED TO VARIOUS CATEGORIES IN PSTC HEALTH BIOTECHNOLOGY GRANTS[1/]

A.

Category	Average % US Budgets	Average % Developing Country Budget	% Total Health Biot Grant Funds
Salary	40.1	37.7	40.7
Equipment	2.8	21.2	16.2
Supplies	14.2	20.7	22.2
Overhead[2/]	13.1	5.7	12.2
Publication/ Bibliographics	1.3	1.0	1.4
Travel	28.1	15.2	8.6
Total Health/Biot Grant Funds	43.7	56.3	

B. Categories of Budget1 Where NO Funds Requested

Category	% US Budgets with NO Request	% Developing Country Budgets with NO Request
Salary	25.0	8.1
Equipment	63.9	18.9
Supplies	33.3	13.5
Overhead	52.8	40.5
Publication/ Bibliographics	50.0	51.4
Travel	13.9	13.5

C. Travel in Joint Budgets[1/] (n=28)

Travel	% US Budgets	% LDC Budgets
None for 1 Collaborator[3/]	8.3	16.0
Greater than 50% of Budget	40.0	12.0

1/ 52.1% of the Health Biotechnology grants have joint budgets (budgets for both U.S. and developing country participants).
The 48 grants studied included 36 US budgets and 37 developing country budgets.

2/ When requested overhead averages 27.3% for US institutions (n=16) compared to 10% for developing country institutions (n=21).

3/ Does not include 10.7% joint budgets with no travel budget for either collaborator.

TABLE 18: SCIENTIFIC PARTICIPATION IN PSTC HEALTH BIOTECHNOLOGY GRANTS (Survey Replies)[1/]

A. Participants in PSTC Health Biotechnology Projects

Status of Participant	U.S.	Developing Country
Ph.D.	8	20
M.D.	4	11
M.Sc.	1	17
Grad. Student	0	24
Technician	6	30
Average reported per grant	2.7	7.3

B. Participant Training in New Techniques

New Technique	Ph.D.	M.D.	M.Sc.	Grad. Stud.	Tech	Total
Antibody Production	5	0	3	3	3	14
Protein Purification	5	2	3	3	3	16
Recombinant DNA	3	4	2	3	1	13
Tissue Culture	2	1	1	3	7	14
Field Testing	0	1	1	0	2	4
Other	0	1	1	0	1	3
Total	15	9	11	12	17	

1/ 14 surveys were received from developing country grantees and 7 surveys were received from U.S. grantees

TABLE 19: PSTC HEALTH BIOTECHNOLOGY GRANT PROJECT OFFICERS

Location	Number Grants
AID/Washington	24
S&T/Health	18
S&T/Agriculture	3
Africa Bureau	1
Asia/Near East Bureau	1
Latin America/Caribbean Bureau	1
AID/Missions	24
Thailand	12
Peru	4
Mexico	1
Burma	1
Philippines	1
Zimbabwe	1
Sudan	1
Sierra Leone	1
Jordan	1
Guatemala	1

1427b

TABLE 20: PROGRESS REPORTS AND EXTENSIONS FOR PSTC HEALTH BIOTECHNOLOGY GRANTS

	% All Grants	% Completed Grants
Extensions[1]	47.9	53.3
Months Completed per Progress Report:[2]		
0-9	50.0	53.3
10-15	20.8	16.7
greater than 15	29.2	30.0

1 The average extension was for 10.6 months.
2 In addition, 53.3% of the completed projects submitted final reports.

1428b

TABLE 20 APPENDIX

Project Number	Grant Months	Extension Months	Months Completed	Completion Date	Progress Reports	Final Report	Total Grant Months Per Progress Rpt.	Peer Reviewed
1.H02	24	3	27	C	1	X	27.0	
2.H01	40	24	64	C	6	X	10.7	X
2.H08	40	45	72	9/89	14		5.1	
2.H12	38	5	43	C	7		6.1	X
2.H13	38	6	44	C	6		7.3	X
2.H14	40	0	40	C	3		13.3	X
3.F04	36	12	48	C	1		48.0	
3.F31	18	12	30	C	2		15.0	X
3.F33	38	6	44	C	6	X	7.3	X
3.F34	38	0	35	11/88	6	X	5.8	
3.F54	22	16	38	C	2	X	19.0	X
3.H09	24	6	30	C	4	X	7.5	X
3.H18	24	0	24	C	5	X	4.8	X
3.H22	24	6	30	C	5	X	6.0	X
3.H24	24	6	30	C	6		5.0	X
3.H33	27	3	30	C	4		7.5	X
4.178	24	5	29	C	4	X	7.2	X
4.227	24	0	24	C	5	X	4.8	
4.321	36	0	36	C	2		18.0	X
4.348	35	12	47	C	1		47.0	
4.410	24	3	27	C	1		27.0	
4.468	35	0	35	C	1		35.0	
4.528	36	0	36	C	6	X	6.0	
4.577	24	0	24	C	6	X	4.0	X
4.607	26	0	26	C	5	X	5.2	
4.633	24	0	24	C	1	X	24.0	X

TABLE 20 APPENDIX

Project Number	Grant Months	Extension Months	Months Completed	Completion Date	Progress Reports	Final Report	Total Grant Months Per Progress Rpt.	Peer Reviewed
5.002	28	0	28	C	3	X	9.3	X
5.038	28	12	37	11/88	1		37.0	
5.052	23	14	37	8/88	3		12.3	
5.130	36	24	15	8/90	1		15.0	
5.140	27	0	27	C	4		6.8	X
5.141	30	0	30	C	5	X	6.0	X
5.148	26	0	26	C	1	X	26.0	X
5.189	40	36	37	11/91	2		18.5	
5.203	29	0	29	C	3		9.7	X
5.221	39	0	36	11/88	3		12.0	
5.224	29	0	29	C	5		5.8	X
5.227	40	12	39	10/89	5		7.8	
5.232	40	3	40	11/88	5		8.0	
6.132	40	0	24	12/89	0		0	
6.225	27	0	24	11/88	1		24.0	
6.299	36	0	24	8/89	2		12.0	
6.317	36	0	23	9/89	1		23.0	
6.345	30	0	26	12/88	2		13.0	
6.390	40	0	24	12/89	3		8.0	
6.391	42	0	26	12/89	4		6.5	
6.392	42	0	26	12/89	3		8.7	
6.419	40	0	24	12/89	4		6.0	